CLINICAL, ELECTROCARDIOGRAPHIC, ECHOCARDIOGRAPHIC AND ANGIOGRAPHIC PROFILE OF ISOLATED LEFT CIRCUMFLEX CORONARY ARTERY DISEASE

Dissertation submitted for

D.M. DEGREE EXAMINATION

BRANCH II – CARDIOLOGY

MADRAS MEDICAL COLLEGE

AND

RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL

CHENNAI – 600 003

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI – 600 032

AUGUST 2012


MADRAS MEDICAL COLLEGE
1835

CERTIFICATE

This is to certify that the dissertation entitled **"CLINICAL, ELECTROCARDIOGRAPHIC, ECHOCARDIOGRAPHIC AND ANGIOGRAPHIC PROFILE OF ISOLATED LEFT CIRCUMFLEX CORONARY ARTERY DISEASE"** presented here is the original work done by **DR. SHANKAR. P.** in partial fulfillment of the requirements for D.M. Branch – II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2012 under my guidance and supervision during the academic period from August 2009 -2012.

Dr.V. KANAGASABAI, M.D.,
THE DEAN
MADRAS MEDICAL COLLEGE & RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL
CHENNAI – 600 003

PROF. V E DHANDAPANI MD, DM.
PROFESSOR AND HEAD OF THE
DEPARTMENT OF CARDIOLOGY
MADRAS MEDICAL COLLEGE &
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL
CHENNAI – 600 003.

DECLARATION

I **Dr. SHANKAR. P** , solemnly declare that this dissertation entitled, **"CLINICAL, ELECTROCARDIOGRAPHIC, ECHOCARDIOGRAPHIC AND ANGIOGRAPHIC PROFILE OF ISOLATED LEFT CIRCUMFLEX CORONARY ARTERY DISEASE"** is a bonafide work done by me at the department of Cardiology, Madras Medical College and Rajiv Gandhi Government General Hospital during the period 2009-2012 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, **Professor V E Dhandapani, M.D.D.M.** This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of **D.M. Degree (Branch II) in Cardiology.**

Dr. SHANKAR. P.

Place : Chennai

Date :

ACKNOWLEDGEMENTS

A great many people made this work possible. I thank my Dean **Dr. V.Kanagasabai, M.D.,** for allowing me to conduct this study.

My warmest respects and sincere gratitude to our beloved **Prof. V E Dhandapani,** Professor and Head of the Department of Cardiology, Government General Hospital, Chennai. But for his constant guidance this study would not have been possible.

My respectful thanks to **Prof R. Subramanian** (Retd.), **Prof GeethaSubramaniam**, (Retd) **Prof Arunachalam** (Retd.), **Prof.M.Somasundaram** (Retd) and **Prof Sundar** (Retd.) for their constructive ideas, personal guidance and involvement in this study.

I am indebted to **Prof. M S Ravi, Prof G Karthikeyan, Prof.Meenaksi, Prof Muthukumar,** and **Prof.Swaminathan**without whom, much of this work would not have been possible.

In addition, I am grateful to D**r.S.Vendkatesan(CoGuide), Dr.G.Gnanavelu,Dr.Ravishankar, Dr.JustinPaul,Dr.C.Elangovan, Dr.G.Prathapkumar, Dr.RajasekarRamesh** and, **Dr Murugan**for helping me during various stages of my study.

Last but not the least I thank all my patients for their kind cooperation.

CONTENTS

Abstract

- The clinical, electrocardiographic, echocardiographic and angiographic profile of 55 patients with isolated left circumflex coronary artery disease (>70% luminal stenosis) were reviewed. The indication for angiogram was documented myocardial infarction in 35 patients (64%) and stable angina pectoris in 20 patients (36%). 30 patients (54.5%) showed Q waves in the resting ECG. Ischemic ST-T changes were noted in 40 patients (72%). RV pattern of ECG changes was noted in 15 patients (27.3%). 27 patients (49%) showed both Q waves and ischemic ST-T changes in their resting ECG. 41 patients (74.5%) among the study population had positive tread mill test. Total number of stenosis noted in left circumflex coronary artery and its branches among the study population was 68. Out of 68 stenosis, 36 (53%) were central and 32 (47%) were periphery. The distribution of central stenosis was proximal LCx 20 (29%), obtuse marginal branches 14 (21%), intermediate 2 (3%). The distribution of peripheral stenosis was distal LCx 30 (44%) and Posterolateral branches 2 (3%). Single stenosis in left circumflex coronary artery and its branches was seen in 43 patients (78%) among the study population. 11 patients (20%) showed double stenosis. Triple stenosis was noted in one patient (2%). The distribution of single stenosis were 23 in central and 20 in peripheral. 20 patients (36%) among the study population had normal EF (>55%). Mild LV dysfunction (EF 46-

55%) was noted in 31 patients (57%) among the study population. Moderate LV dysfunction (EF 30-45%) was noted in 4 patients (7%). Mild mitral regurgitation was noted 4. patients (7.2%) Average risk factor is 2.8 per patient. Number of patients with no risk factor is 2 (4%), single risk factor is 5 (9%) and those with multiple risk factors is 48 (87%) patients. ECG changes in lateral leads are common is patients with stenosis in proximal LCX. ECG changes in inferior leads are common in patients with stenosis in distal LCX. Central stenosis involving proximal LCX is more common in patients with documented evidence of MI.

- Keywords: Isolated circumflex coronary artery disease. Coronary angiogram.

INTRODUCTION

Isolated left circumflex coronary artery disease is uncommon and occurs in a small percentage of patients undergoing coronary angiogram. Because of the rarity of isolated coronary artery disease not many studies involving isolated coronary artery disease are available in literature. Clinical, electrocardiographic, Echocardiographic and angiographic features of these patients with isolated left circumflex coronary artery disease is therefore, poorly characterised. Occlusion of LCX may be associated with an electrocardiographic pattern of inferior myocardial infarction, similar to the feature of right coronary artery occlusion. Patients with isolated LCx-related infarction have different patterns of myocardial damage. As the amount of myocardium in jeopardy is proportional to the sum of the amount of myocardium distal to each lesion in the coronary artery tree, and the effectiveness of interventional therapy appears to be more significant in larger than in smaller myocardial injuries independent of the site of infarction, it is pertinent to assess the relation of ECG patterns to the site of coronary stenosis and the status of left ventricular function in patients with isolated LCx disease with or without myocardial infarction.

AIM OF STUDY

To study the clinical presentation of patients presenting with isolated left circumflex coronary artery disease.

To determine the specific electrocardiographic changes in isolated left circumflex coronary artery disease.

To determine the relationship between site of stenosis (central vs peripheral) and electrocardiographic patterns.

To determine the association between the location and extent of stenosis in isolated left circumflex coronary artery disease and left ventricular systolic function.

To study the Echocardiographic features associated with left circumflex coronary artery disease.

To study the prevalence of risk factors in patients with isolated left circumflex coronary artery disease.

REVIEW OF LITERATURE

Isolated left circumflex coronary artery (LCx) disease[1] is uncommon and occurs only in few patients at angiography. The clinical, electrocardiographic, echocardiographic and angiographic features for these patients, therefore, remain poorly characterized. Occlusion of the LCx[2] may be associated with an electrocardiographic (ECG) pattern of inferior myocardial infarction similar to the feature of right coronary artery occlusion or high lateral wall MI. Patients with LCx-related infarction[3] have different patterns of myocardial damage. As the amount of myocardium in jeopardy is proportional to the sum of the amount of myocardium distal to each lesion in the coronary artery tree, and the effectiveness of interventional therapy appears to be more significant in larger than in smaller myocardial injuries independent of the site of infarction, it is pertinent to assess the relation of ECG patterns to the site of coronary stenosis[4] and the status of left ventricular function in patients with isolated LCx disease.

Risk scores in acute coronary syndrome

The integration of underlying risks of coronary artery disease and risks of thrombosis is potentially challenging at the bedside. Accordingly, there is a need for simplified and widely applicable risk stratification tools

facilitating the triage and management of patients with ACS. The simplest risk scoring systems have demonstrated that, in population analyses, a simple composite of age, systolic blood pressure and heart rate provides valuable prognostic information for patient groups. However, this information is less accurate and predictive for individual patients.

Relationship between anatomy of occlusion, ECG changes and 1-year mortality in acute MI

Location	Anatomy of occlusion	ECG	1-year mortality (%)
Proximal left anterior descending	Proximal to first septal perforator	ST↑ V1–6, I, aVL and fascicular bundle or bundle branch block	25.6
Mid left anterior descending	Proximal to large diagonal but distal to first septal perforator	ST↑ V1–6, I, aVL	12.4
Distal left anterior descending or diagonal	Distal to large diagonal or to diagonal itself	ST↑ V1–V4 or ST↑ I,V5,6 aVL, V5–V6	10.2
Moderate to large inferior (posterior, lateral, right ventricular)	Proximal right coronary artery or left circumflex	ST↑ II, III, aVF and any or all of the following: 1) V1, V3R, V4R 2) V5V6 3) R > S in V1, V2	8.4
Small inferior	Distal righ coronary artery or left circumflex branch occlusion	ST↑ II, III, aVF only	6.7

TIMI risk score

Based upon data from clinical trials, the TIMI risk score[5]was derived and tested in STEMI populations. This score allocates points on the basis of age, history of diabetes, hypertension or angina and examination features including blood pressure, heart rate, Killip class[6] and weight. It also includes ST-segment elevation or left bundle branch block

on the ECG and time to reperfusion of <4 hours. This score provides a simple and practical bed side tool for the triage of patients into high-risk, moderate-risk, or low-risk categories. In NSTEMI, the TIMI risk score was less accurate in predicting death. The PREDICT score[7] includes assessment of left ventricular function on discharge, with improved predictive accuracy.

GRACE risk score[8]

Based upon a large unselected registry population of the full spectrum of ACS, eight variables were derived within dependent predictive power for in-hospital death and for post-discharge death or myocardial infarction at6 months post-discharge. The data were tested prospectively and against an external dataset (GUSTO-IIB). The eight variables contain more than 90% of the predictive capacity of the full multivariable model. The score can be used to provide a numerical risk of in-hospital death or post-discharge death or MI based upon a score card or using software running on palm devices or personal computers. Thus, although the contributions of individual risk factors are difficult to estimate at the bedside for each individual patient, newly established risk-score tools provide simple methods to estimate the risk of death and MI, and hence guide in-hospital and post-discharge management.

Imaging modalities in ACS

Imaging modalities are secondary tools in the diagnosis of ACS. They usually only confirm or exclude the working diagnosis based on clinical presentation, biochemical markers and the ECG.

Coronary angiography

This is the gold standard to prove or exclude coronary artery disease. In approximately 10–15% of patients presenting with chest pain no high-grade lesion can be identified, or coronary artery disease is excluded. The extent and location of lesions is useful for risk assessment and decision-making concerning revascularization by means of angioplasty or surgery. The culprit lesions that are responsible for the clinical symptoms frequently show filling defects, indicating intracoronary thrombus formation.

Echocardiography

Left ventricular systolic function is an important prognostic variable in patients with ischaemic heart disease and can easily and accurately be assessed by echocardiography. Two-dimensional echocardiography in experienced hands is a useful bedside technique in the triage of patients with acute chest pain. Regional wall-motion abnormalities occur within

seconds after coronary occlusion well before necrosis. However, these are not specific for acute events and may be the result of old infarctions. Transient localized hypokinesia or akinesia in segments of the left ventricle wall may be detected during ischaemia,with normal wall motion on resolution of ischaemia. The absence of wall-motion abnormalities excludes major myocardial infarction. Echocardiography is of additional value for the diagnosis of other causes of chest pain such as acute aortic dissection, pericardial effusion, or massive pulmonary embolism.

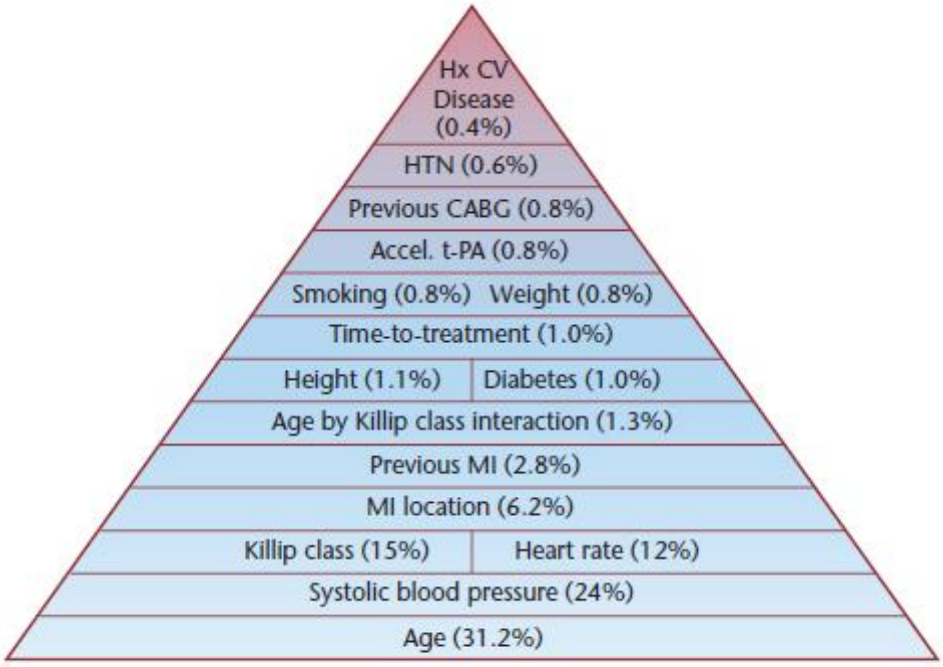
The long-term risk of mortality is related to well established parameters. These include age and the established risk factors. From imaging modalities the extent of coronary artery disease (main stem lesion) and reduced left ventricular function are predictors of future outcome. Biochemical markers of inflammation (CRP) and of renal insufficiency (creatinine clearance) are further strongly associated with increased mortality.

Risk stratification in ST-segment elevation myocardial infarction

Whereas risk factors for the development of atherothrombosis provide insights into disease mechanisms and the opportunity for primary and secondary prevention therapy, analysis of the risk for adverse outcome

after presentation with ST-segment elevations is critically important in guiding management and therapeutic decisions. Analysis usually uses a combination of clinical, ECG and biochemical parameters. Five rather simple baseline parameters can be used to predict more than 90% of the 30-day mortality: age, systolic blood pressure, Killip class, heart rate and infarct localization[12].

Multivariate model of 30-day mortality in acute MI according to GUSTO Itrial.



Killip class

The haemodynamic impact of the evolving myocardial infarction is clinically evident by the symptoms of shock. The Killip classification is

widely used and linked to outcome. Killip class IV (‘cardiogenic shock’) is found in about 5% of AMI patients and is associated with extremely high mortality.

Infarct location

The prognosis of myocardial infarction is related to the extent of myocardium at risk and, related to this, to the site of coronary occlusion. The ECG reflects the infarct location. Patients with main stem occlusion only rarely reach the hospital for reperfusion therapy. Occlusion of the proximal left anterior descending coronary artery proximal to the first septal branch is associated with high early and late mortality (‘widow-maker’). Large inferior myocardial infarctions as a result of occlusion of a dominant right coronary artery are also a high risk, particularly when the right ventricle is involved. Other locations, such as apical (distal left anterior descending), lateral (diagonal branch), or small inferior infarctions (distal right or circumflex), show ST-segment elevations in only a few leads and have a better outcome. Strictly posterior myocardial infarctions (marginal branch of left circumflex) may escape routine ECG leads or only be evident through ST depression in V1 to V4, but usually have a good outcome.

ECG criteria

The ECG allows the rough location of the infarct artery and identification of the extent of the territory at risk. The development of a bundle branch block or atrioventricular block in anterior myocardial infarctions suggests involvement of a proximal septal artery and is associated with increased mortality. Atrioventricular blocks in inferior myocardial infarctions are frequent and mostly transient.

Biomarkers on presentation

Blood sampling for serum markers must be routinely performed in the acute phase, but one should not wait for the results to initiate reperfusion treatment. The finding of elevated markers of necrosis may sometimes be helpful in deciding to give reperfusion therapy (e.g. in patients with left bundle branch block), but should retard decision making. Elevation of markers of necrosis (troponin) on arrival in hospital is associated with adverse outcome[13].

Parameters of high acute risk
Recurrent ischaemia /chest pain
Dynamic ST-segment changes
Elevated biomarkers: troponin, BNP
Haemodynamic instability
Major arrhythmias (VF, VT)
Diabetes

Ischaemic cardiomyopathy

In a number of cases the clinical presentation of chronic stable IHD is dominated by symptoms and signs of left ventricular dysfunction, a condition defined as ischaemiccardiomyopathy[13.] This is the most common form of dilated cardiomyopathy and most often occurs in patients with a history, or evidence, of previous myocardial infarction[14.] Concomitant stable angina can be present in some of these patients. Ischaemic cardiomyopathy can result from a single large infarction (usually >20% of myocardial mass) or from multiple smaller infarctions, followed by progressive ventricular dilatation and dysfunction, which may develop over a number of years. The reasons why for a similar extent of myocardial

infarction some patients, but not others, develop severe myocardial dysfunction are still largely debated[15]. Notably; some patients may have suffered from one or more silent myocardial infarctions, revealed by pathological Q waves on a routine ECG, developing symptoms of heart failure as the first manifestation of IHD. In other patients there is no clinical and ECG evidence of previous myocardial infarction, suggesting progressive ischaemia related loss of myocytes, possibly involving apoptosis. Symptoms of left ventricular dysfunction typically include dyspnoea on effort, paroxysmal nocturnal dyspnoea, fatigue, weight gain and reduced urinary output. Physical examination may reveal signs of heart failure, including a reduced first heart sound, presence of a third sound, ankle oedema and pulmonary rales. A systolic murmur can be present when mitral regurgitation occurs as a consequence of left ventricular dilatation or papillary muscle dysfunction. Echocardiography shows left ventricular dilatation and reduced ejection fraction and, frequently, severe diastolic dysfunction. Coronary angiography usually exhibits multivessel coronary artery disease. In some patients the extent and severity of coronary atherosclerosis is much less than predicted by left ventricular dysfunction, thus suggesting that the latter could mainly be caused by a primary myocardial disease, such as myocarditis. Ischaemic cardiomyopathy is associated with a poor outcome, compared to stable

IHD without severe impairment of left ventricular function. The reasons for the worse clinical outcome include higher risks of (1) life-threatening ventricular arrhythmias, (2) severe left ventricular dysfunction during recurrence of ischaemia or a new myocardial infarction, (3) potentially fatal systemic complications, and (4) iatrogenic complications as a result of the multidrug therapy.

Electrocardiographic pattern of ischaemia, injury and necrosis

The ionic changes, pathological alterations and electrophysiological characteristics that accompany different stages of clinical ischaemia/infarction are well known. The classic ECG sequence that appears in cases of complete coronary occlusion is as follows. The ECG pattern of subendocardial ischaemia (increase of T-wave amplitude) appears first[16]. When the degree of clinical ischaemia is more important, the pattern of injury (ST segment elevation) is present. Finally, necrosis of the myocardium is indicated by the development of a Q-wave pattern.

Electrocardiographic pattern of ischaemia

From an experimental perspective, ischaemia may be subepicardial, subendocardial or transmural. From the clinical point of view, only

subendocardial and transmural ischaemia exist and the latter presents the morphology of ‘subepicardial’ ischaemia owing to the proximity of the subepicardium to the exploring electrode.

Experimentally and clinically, the ECG pattern of ischaemia (changes in the T wave) may be recorded from an area of the left ventricular subendocardium or subepicardium in which ischaemia induces a delay in repolarization. If the ischaemia is subendocardial, a more positive than normal T wave is recorded; in the case of subepicardial ischaemia (in clinical practice transmural), flattened or negative T waves are observed. The negative T wave of subepicardial ischaemia (clinically transmural) is symmetric, usually with an isoelectric ST segment. It is a common finding, especially in the long term after a Q-wave myocardial infarction. It may also be a manifestation of acute coronary syndrome (ACS).In contrast, an increase in T-wave amplitude, a common feature of subendocardial ischaemia, is recognized less frequently and the difficulty of diagnosis is increased because of its transient nature. It is observed in the initial phase of an attack of Prinzmetal angina and occasionally in the hyperacute phase of ACS. Sometimes, it is not easy to be sure when a positive T wave may be considered abnormal. Therefore, sequential changes should be evaluated.

Electrocardiographic pattern of injury

Experimentally and clinically, the ECG pattern of injury (changes in the ST segment) is recorded in the area of myocardial subendocardium or subepicardium where diastolic depolarization occurs as a consequence of a significant decrease in blood supply. In the leads facing the injured zone, ST depression is recorded if the current of injury is dominant in the subendocardium (ECG pattern of subendocardial injury), while ST elevation is observed if the current of injury is subepicardial (clinically transmural - ECG pattern of subepicardial injury). Mirror image patterns also exist, for example if subepicardial injury occurs in the posterior part of the lateral wall of the left ventricle, ST-segment elevation will be observed in the leads on the back while ST depression will be seen in V1–V2 as a mirror image. Also, the mirror images, or reciprocal changes, are very useful for locating the culprit artery and the site of the occlusion.

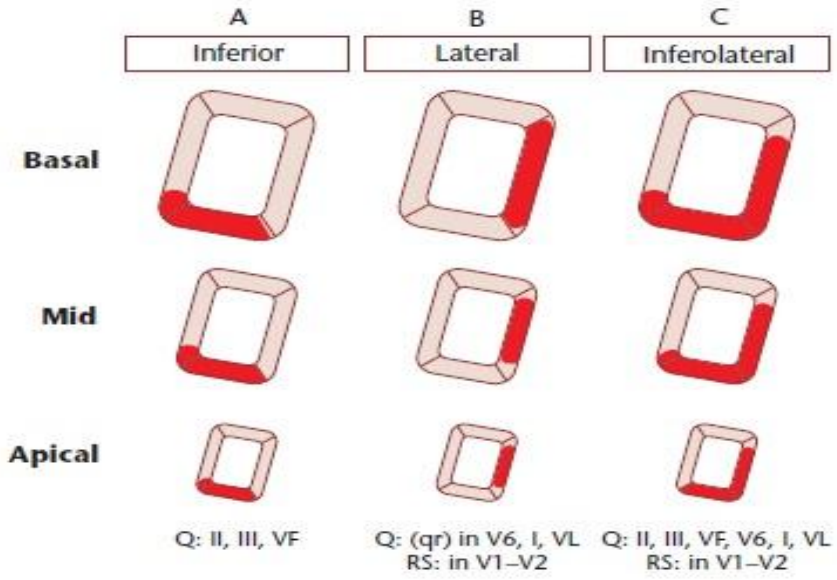
LAD artery occlusion leads to ST-segment elevation[18] predominantly in precordial leads[17], while right coronary artery (RCA) or left circumflex (LCX) artery occlusion gives rise to ST-segment elevation in the inferior leads. The extent of myocardium at risk can be estimated based on the number of leads with ST changes(‘ups and downs’). This approach has some limitations, especially related to the pseudo-normalization of ST changes in the right precordial leads that often occurs when the RCA occludes prior to the origin of the right ventricular artery.

Proximal LAD occlusion (before the first diagonal and septal arteries) as well as RCA occlusion proximal to the right ventricular artery have a poor prognosis. It is therefore useful to predict the site of occlusion in the early phase of ACS to enable decisions regarding the need for urgent reperfusion strategies. Careful analysis of ST changes in the 12-lead ECG recorded at admission may predict the culprit artery and the location of the occlusion.ST elevation is found in leads that face the head of an injury vector, while in the opposite leads ST depression can be recorded as a mirror image.

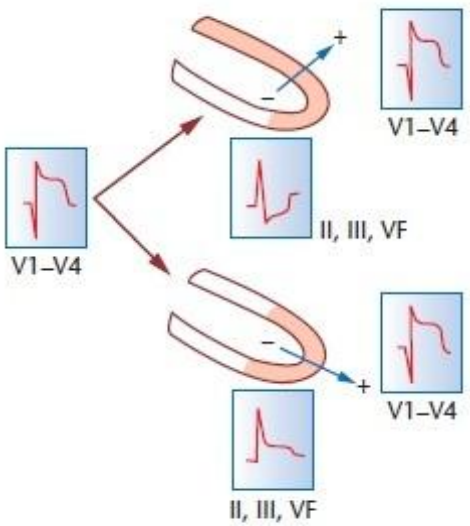
The right ventricular involvement that usually accompanies proximal RCA occlusion may be shown by ST changes in the right precordial leads (V3R, V4R)[19]. ST-segment changes in these leads, though specific, disappear early during the evolution of myocardial infarction. Furthermore, these leads are often not recorded in emergency rooms. Thus, the real value of these changes is limited and in order to identify the culprit artery (RCA or LCX) in the case of an acute inferior myocardial infarction.

The criterion of isoelectric or elevated ST in V1 has the highest accuracy in predicting proximal RCA occlusion[20.] In these cases the ST elevation in V1 may also occur in V2 or V4 but with a V1/V3–4 ratio over 1. This differentiates these cases from cases of antero-inferior infarction[18]., in which there is also ST elevation in inferior and precordial leads but the ST elevation V1/V3–4 ratio is less than 1.

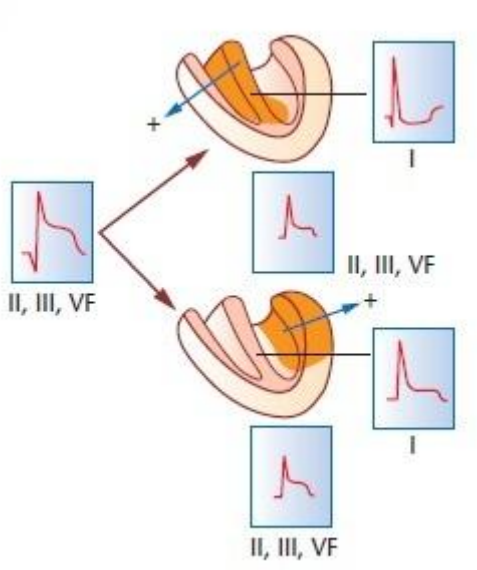
Anatomical–ECG correlations in myocardial infarction affecting (A) inferior wall, (B) lateral wall and(C) the entire inferolateral zone.



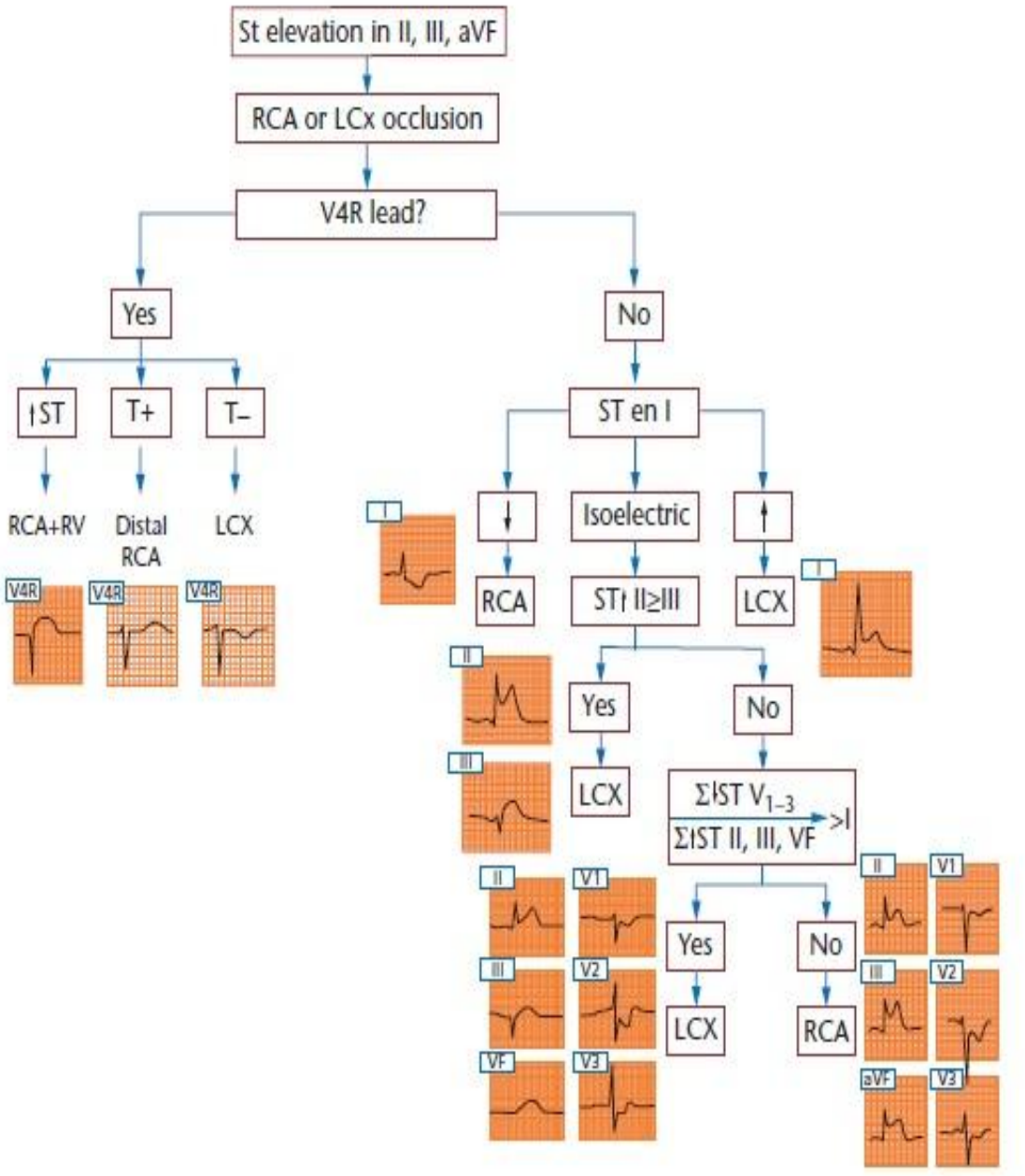
ST elevation in precordial leads: as a consequence of occlusion of the left anterior descending artery (LAD), the ST changes in reciprocal leads (II, III, VF) allow identification of the site of occlusion, i.e. proximal LAD shows ST depression or distal LAD shows ST elevation in inferior leads.



ST elevation in inferior leads (II, III, aVF): the ST changes in other leads, in this case lead I, provide information on whether the inferior infarction is likely to be due to occlusion of the right coronary artery (ST depression) or left circumflex artery (ST elevation).



Algorithm for locating occlusion of right coronary artery (RCA) or left circumflex artery (LCx) in evolving myocardial infarction with ST elevation (STEMI) in inferior leads.



VALUE OF ST-T SEGMENT CHANGES IN LEAD V_4R IN ACUTE INFERO-POSTERIOR MYOCARDIAL INFARCTION

ST↗ ≧ 1 mm
POS T-WAVE

PROXIMAL OCCLUSION RCA

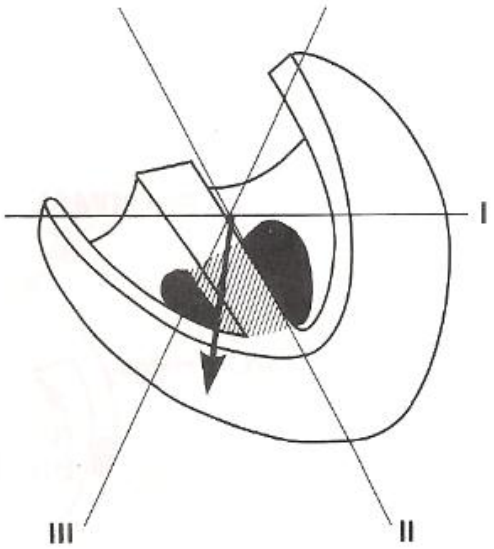
NO ST↗:
POS T-WAVE

DISTAL OCCLUSION RCA

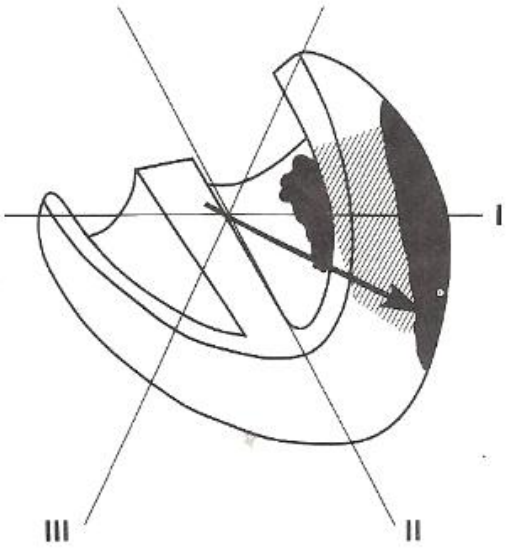
NEG T-WAVE

OCCLUSION CX

RIGHT CORONARY ARTERY MI



CIRCUMFLEX CORONARY ARTERY MI



ST SEGMENT VECTOR IN RIGHT CORONARY ARTERY
VS CIRCUMFLEX MYOCARDIAL INFARCTION

Relationship between infarcted area, ECG pattern, name given to infarction and the most probable culprit artery and place of occlusion. (LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery)

Type of MI		Infarction area (CMR)	ECG pattern	Name given to MI	Most probable place of occlusion
ANTEROSEPTAL ZONE	A1 n=7		Q in V1–2 SE: 86% ES: 98%	Septal	LAD 
	A2 n=7		Q in V1–2 to V4–V6 SE: 86% ES: 98%	Apical/ anteroseptal	LAD 
	A3 n=6		Q in V1–2 to V4–V6 I and VL SE: 83% ES: 98%	Extensive anterior	LAD 
	A4 n=4		Q (qs or r) in VL (I) and sometimes V2–3 SE: 70% ES: 100%	Limited anterior	LAD 
INFEROLATERAL ZONE	B1 n=6		Q (qr or r) in I, VL, V5–6 and/or RS in V1 SE: 50% ES: 98%	Lateral	LCX 
	B2 n=8		Q in II, III, VF SE: 87.5% ES: 98%	Inferior	RCA LCX 
	B3 n=10		Q in II, III, VF (B2) + Q in I, VL, V5, 6 and / or RS in V1 (B1) SE: 70% ES: 100%	Inferolateral	

General risk factors for acute coronary syndromes

A series of modifiable risk factors (e.g. hyperlipidaemia, hypertension, diabetes and metabolic syndrome) and non-modifiable risk factors (e.g. gender and age) relate to the development of atherosclerosis and the risk of presenting with ACS.

Age and gender

The most powerful independent predictor for the development of ACS, including presentation with myocardial infarction, is age. Among men, risk increases with each decile of age and comparisons between men and women demonstrate that for premenopausal women the risk corresponds with that of men approximately 10 years younger[21]. Post menopause, the risks increase for women but remain lower than for men of corresponding age. However, interpretations of the impact of gender in ACS are complex and potentially influenced by referral bias and by differences in diagnostic sensitivity of the ECG and stress tests with gender. On angiography of suspected ACS a higher proportion of women do not have significant obstructive coronary heart disease. Adjusted for age, women have higher rates of diabetes and hypertension but are less frequently smokers[22.]

Family history

Having accounted for all known risk factors, family history remains a significant independent risk factor for the development of coronary heart disease. In addition, genetic traits contribute to the specific risk phenotypes, including those related to hyperlipidaemia and hypertension. Twin studies reveal higher concordance among identical than non-identical twins.

Diabetes and metabolic syndrome

Clinical and animal studies demonstrate the importance of diabetes as a risk factor for the development of atherosclerosis as well as for ACS, and the increasing prevalence of obesity in specific populations is implicated in the increased frequency of metabolic syndrome and type 2 diabetes. Patients with type 2 diabetes mellitus have a risk of death from cardiovascular causes that is two- to six fold elevated compared to those without diabetes. The development of ACS or cardiovascular death accounts for more than one-quarter of all new cardiovascular events among those with diabetes. Intensive intervention involving multiple risk factor reduction among patients with type 2 diabetes and microalbuminuria demonstrates that five patients need to be treated to prevent one cardiovascular event over the course of 8 years[23].The dramatic increase in

the prevalence of obesity among children and adolescents has been demonstrated across many economically developed and developing communities. This rise has serious implications for future coronary events, including ACS. Among obese children and adolescents, the prevalence of metabolic syndrome approaches 50% (38.7% in moderately obese subjects and 49.7% in severely obese subjects)[24]. C-reactive protein (CRP) and interleukin-6 are markers of inflammation and their levels can be used as predictors for future cardiovascular events; the concentrations of these markers rise with the extent of obesity. In addition, adiponectin, a biomarker of insulin sensitivity which also has a role in preventing atherosclerosis development, is decreased in obesity. The findings provide a link between obesity, metabolic syndrome and future risk of acute coronary events. In the third National Health Nutrition Examination Survey (TNHNES) of more than 10 000 subjects, the presence of the metabolic syndrome independently increased the risk of myocardial infarction twofold[25]. Other independent predictors of cardiac events were low levels of high-density lipoprotein (HDL)-cholesterol), hypertension and hypertriglyceridaemia. A target-driven long-term intensified intervention aimed at modifying several risk factors in patients with type 2 diabetes and microalbuminuria reduces the risk of cardiovascular and microvascular events by approximately50%[24].

Hypertension

There is a strong association between hypertension and coronary heart disease and there is a particularly strong influence of elevated blood pressure on stroke. Approximately two-thirds of cerebrovascular disease burden and half of ischaemic heart disease burden are attributable, at least in part, to elevated blood pressure[26].“The Blood Pressure Lowering Treatment Trialists” collaboration has examined the influence of blood pressure lowering on mortality and the development of major cardiovascular events[27] .The overview examined data from 29 randomized trials and the key finding was that the larger the reduction in blood pressure (irrespective of the regimen used) the greater the reduction in risk of cardiovascular events. Thus, blood pressure lowering is critically important not only in secondary prevention but in the primary prevention of major cardiovascular events including the development of ACS.

Lipid abnormalities

Extensive studies have demonstrated that elevated low-density lipoprotein (LDL) cholesterol and very-low-density lipoprotein (VLDL) cholesterol are associated with atherogenesis and that lowering total cholesterol and LDL cholesterol is associated with reduced atherogenesis. Reduced cardiovascular complications have been demonstrated in primary

and secondary prevention clinical trials[28]. Elevated levels of HDL-cholesterol are protective whereas reduced levels of HDL confer increased risk. Multiple large-scale cholesterol-lowering trials have demonstrated a reduced number of cardiovascular events among treated individuals without manifest coronary artery disease at the time of inclusion (WOSCOPS, AFCAPS, TEXCAPS). Among those patients with hypertension at baseline, a 3-year treatment with a statin (atorvastatin) reduced the risk of major cardiovascular events by approximately one-third.

Other modifiable and potentially modifiable risk factors

Up-regulation of systemic inflammation provides a plausible mechanism for accelerating atherogenesis and its acute complications. A series of risk factors may be directly or indirectly related to increased coronary and vascular risk (for example elevated homocysteine, CRP, fibrinogen, plasminogen activator inhibitor type 1 and altered platelet reactivity). A series of additional 'environmental factors' are influenced by life-style but may also interact with the genetically influenced factors listed above. These include high-fat, low-antioxidant diets (experimentally and clinically), smoking, a lack of exercise, and obesity. Infectious agents may also contribute to the up-regulation of the inflammatory response and

acceleration of atherogenesis. Individuals born with low birth weight exhibit a two to threefold increased risk in later life of non-fatal coronary heart disease compared with normal birth weight infants. Low birth weight is also associated with several coronary risk factors including the subsequent development of hypertension, type 2 diabetes and elevated cholesterol and fibrinogen concentrations. The risk factors are related not only to birth weight but to other indicators of restriction of fetal growth including small head circumference and altered placental development. The associations between size at birth and coronary heart disease are not explained by premature birth. They are also independent of the risks of subsequent obesity, smoking and socioeconomic classification. The findings have led to the hypothesis that coronary heart disease is programmed in fetal life[29] ('the Barker hypothesis'). *In-utero* programming of steroid metabolism may explain, at least in part, the re-setting of vascular tone in the arterial system and insulin sensitivity. Based upon the INTERHEART[30] case–control study in 52 countries, nine potentially modifiable risk factors account for more than 90% of the risk of AMI, consistently across geographic regions and ethnic groups. Identified risk factors include abnormal lipids reflected by the apolipoprotein B–apolipoprotein A1 ratio, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits and vegetables,

alcohol and regular physical activity. The findings suggest that these phenotypes are potentially amenable to modification across countries and diverse ethnic populations. This has major implications for primary and secondary prevention strategies.

Clinical presentation

An accurate history is essential in distinguishing the onset of ACS from alternative diagnoses. The prodrome is characterized by anginal type chest discomfort, but usually at rest or on minimal exertion. Of patients with STEMI and prodromal symptoms, two-thirds have symptoms in the preceding week and one-third have symptoms for up to 4 weeks. Overall, only 20% have symptoms for less than 24 hours. The clinical presentation of patients with ACS encompasses a large variety of symptoms. The cardinal symptom is the ischaemic chest pain which is typically described by the patient as burning, tightness, or heaviness. Patients often have associated symptoms of nausea and fatigue. Chest pain can be graded according to the Canadian Cardiovascular Society Classification (CCS).To recognize subgroups of patients with unstable angina who are at different levels of cardiac risk, the Braunwald classification was introduced[31]. This empirically developed classification is based on symptoms with respect to

pain severity and duration as well as the pathogenesis of myocardial ischaemia and was validated in prospective studies[32] .

Patients with STEMI usually have severe chest pain with fear of dying, whereas in non-ST elevation ACS the pain is more waning and waxing, is dependent on the level of exertion, but usually lasts no longer than 20 minutes. The pain is typically located in the centre or the left lateral chest and radiates to the left shoulder, arm, neck and jaw. Pain may also be epigastric, particularly in inferior myocardial infarctions. Perception of pain in the right side of the chest does not exclude myocardial ischaemia. If the pain is related to inspiration (pleuritic pain), or radiates to the back, other differential diagnoses including aortic dissection must be considered. Pain that persists over many days or pain that can be provoked mechanically is not ischaemic. In up to one-half of patients with STEMI physical and or emotional factors are identified in the prodrome and may have influenced plaque rupture. A circadian periodicity of presentation with STEMI is observed. The peak incidence of events coincides with the early waking hours, possibly associated with rises in catecholamine sand cortisol and increases in platelet aggregability. Population studies reveal that approximately 30% of myocardial infarctions occur silently or with less severe symptoms. They are detected only by chance on subsequent ECG recordings[33] .Atypical presentations of

ACS are not uncommon. They are often observed in younger (25–40 years) and older (>75 years) patients, diabetic patients and in women. In the Multicenter Chest Pain Study, acute myocardial ischaemia was diagnosed in 22% of patients presenting to emergency departments with sharp or stabbing chest pain, 13% of those with chest pain that had some pleuritic features, and in only 7% of those whose chest pain was fully reproduced by palpation. In addition, variant angina, as a result of coronary spasm, forms part of the spectrum of unstable angina and may not be recognized at initial presentation. Accordingly, the assessment of clinical symptoms alone is insufficient for risk stratification as symptoms may be difficult to assess objectively and can easily be subject to misinterpretation.

Echocardiography

Left ventricular systolic function is an important prognostic variable in patients with ischaemic heart disease and can easily and accurately be assessed by echocardiography. Two-dimensional echocardiography in experienced hands is a useful bedside technique in the triage of patients with acute chest pain. Regional wall-motion abnormalities occur within seconds after coronary occlusion well before necrosis. However, these are not specific for acute events and may be the result of old infarctions.

Transient localized hypokinesia or akinesia in segments of the left ventricle wall may be detected during ischaemia, with normal wall motion on resolution of ischaemia. The absence of wall-motion abnormalities excludes major myocardial infarction. Echocardiography is of additional value for the diagnosis of other causes of chest pain such as acute aortic dissection, pericardial effusion, or massive pulmonary embolism.

Echocardiography in Acute MI

Urgent transthoracic 2-D echo can play a crucial role in establishing the diagnosis of acute MI, determining its location, extent and prognosis. Regional wall motion abnormality (RWMA) is the echocardiographic hallmark of an acute MI. The extent of RWMA is directly related to the volume of myocardium in jeopardy. RWMA in classic inferior MI involves segments bordering posterior interventricular grove with variable amounts of involvement of inferoposterior wall. RWMA in classic anterior MI involves anterior septum, anterior wall and apex. Circumflex coronary artery occlusion involves RWMA in inferior, posterior and posterolateral wall.

There are several nonischemic causes of RWMA which may complicate analysis. These include LBBB and post-operative (CABG or other cardiac surgery). Multiple studies have validated the clinical utility

of 2-D echo for detecting wall motion abnormalities in suspected acute MI setting. In general 80% to 95% of patients with documented MI will have detectable RWMA. Experimentally there is a threshold of myocardium required to produce a RWMA. It also appears that there is a total myocardial burden that must be rendered ischemia before a RWMA develops. For this reason, MI involving exceptionally small territories may not result in detectable RWMA. In contemporary practice, resting transthoracic ECHO is rarely used as a stand-alone technique in patients presenting with chest pain syndromes.

Natural history of wall motion abnormalities

Transthoracic ECHO can be used to follow the progression or regression of wall motion abnormalities. If successful reperfusion id obtained either by catheter-based or pharmacologic strategies, wall motion abnormality recovers fully or in part in most patients. If there is a delay in institution of reperfusion strategies, many patients will be left with varying degrees of nontransmural myocardial fibrosis. Because of residual fibrosis, wall motion abnormalities may persist in these patients. Without successful restoration of flow, natural course of acute MI is far a variable degree of transmural necrosis to occur depending on completeness of coronary occlusion and the presence of coronary collateral circulation. In this

instance , there will be no recovery of function in the infarct zone. The border zones that may have compromised myocardial perfusion acutely and hence have abnormal wall motion may show recovery of function. However, the central transmural infarct zone will remain akinetic. Over a 6-week period, myocardial necrosis is replaced by fibrosis and scar. Both pathologically and echocardiographically, the wall becomes thinner and denser.

Prognostic Implications

Many studies have demonstrated the adverse prognosis of wall motion abnormalities in patients presenting with MI. In general, the more extensive the wall motion abnormality, greater is the likelihood of complications such as congestive cardiac failure, arrhythmia and death. The extent of regional wall motion abnormality can be accurately quantified by wall motion score. In the presence of isolated single vessel coronary artery disease, normally there is compensatory hyperkinesis of remaining segments. Failure to develop compensatory hyperkinesis is a marker of multivessel CAD.

Wall motion score

The quantitation of wall motion abnormalities involves generation of wall motion score or score index. This involves describing the wall motion characteristics of each of the predefined segments as being normal, hypokinetic, akinetic and dyskinetic or aneurysmal. A numerical score is applied to each of these segments. The total score is divided by the number of the segments evaluated to create a wall motion score index[34]. A ventricle with a completely normal wall motion has a wall motion score index of 1.0. Higher scores represent progressively greater degrees of ventricular dysfunction.

Wall motion score
1= Normal
2= Mild hypokinesia
3= Severe hypokinesia
4= Akinesia
5= Dyskinesia

Complications of acute MI

Virtually all mechanical complications (acute MR,VSR, free wall rupture) of acute MI can be diagnosed with 2-D echo. In most cases, routine transthoracic scanning suffices for this assessment. Colour Doppler

flow imaging is crucial for detection and quantitation of lesions such as MR and VSR.

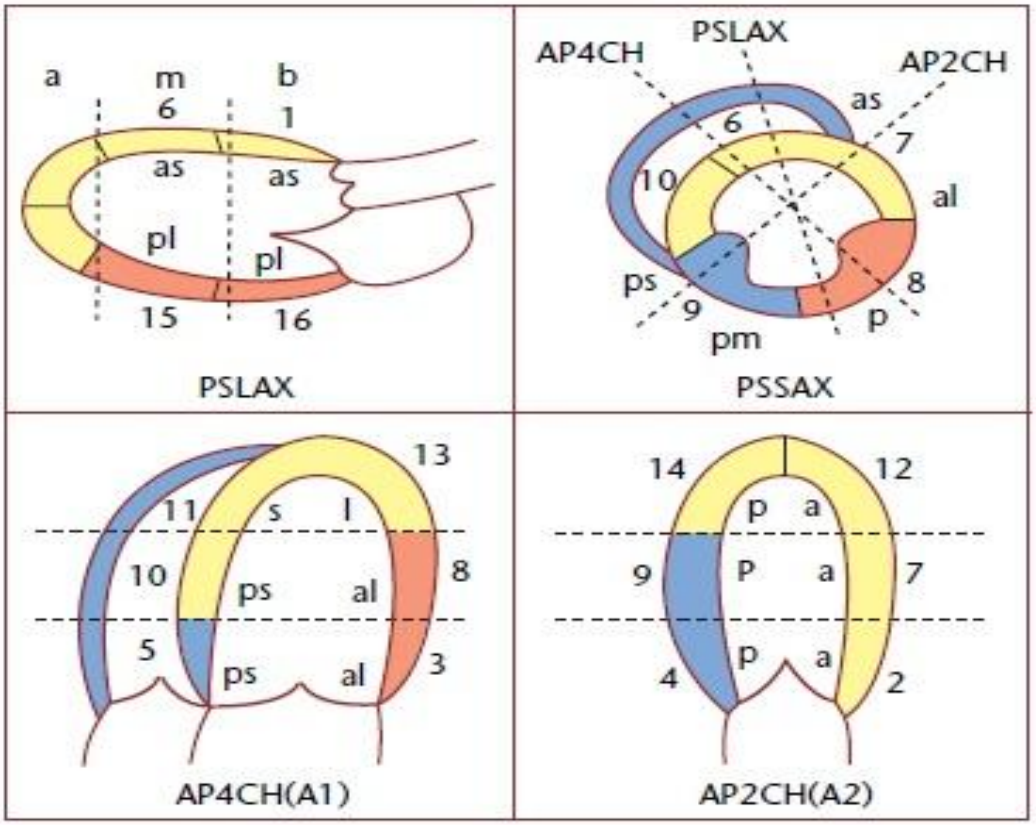
Ischaemic heart disease

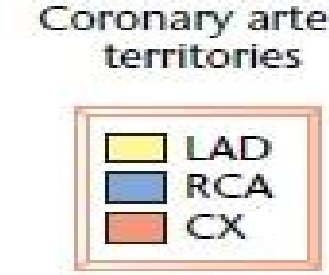
Reduction in myocardial blood flow causes ischaemia with decreased wall thickening/function followed by ECG changes and chest pain. Echocardiography allows detection of transient regional wall motion abnormalities during episodes of chest pain and has been shown to be extremely helpful for the assessment of patients presenting with chest pain and acute coronary syndrome. Demonstration of completely normal wall function/motion during such an episode virtually excludes myocardial ischaemia or myocardial infarction. This wall-motion assessment is very useful in patients presenting with chest pain and a non-diagnostic ECG. In addition, echocardiography and Doppler allows diagnosis of most diseases that can mimic ischaemic episodes. Unstable angina is characterized by transient or permanent wall motion abnormalities. Myocardial infarction results in a permanent reduction in wall thickness (<6 mm), which is replaced by fibrotic/scar tissue. Outward systolic motion or bulging results in an abnormal ventricular shape and indicates aneurysm formation. Free-wall rupture after pericarditis with epicardial and pericardial adhesion results in a pseudo or false aneurysm. Both types of aneurysm contain

thrombus but a true aneurysm leads more often to systemic embolization. RV infarct involvement is also readily detected (RV dilatation). The detection of complications of a myocardial infarction is the domain of bedside echocardiography. Ventricular septal rupture and papillary muscle rupture are readily diagnosed. Chronic complications include thrombosis, aneurysm formation and remodelling with heart failure, all of which are readily diagnosed by echocardiography

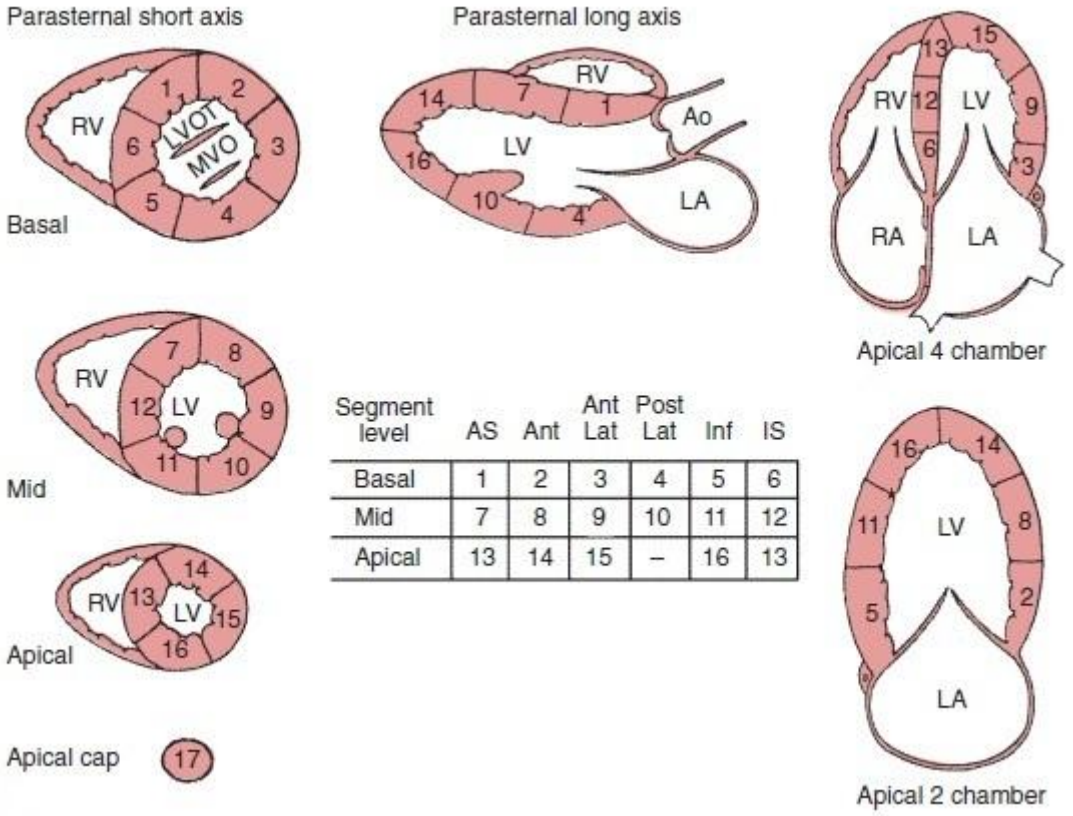
.

Method for standardized qualitative wall motion analysis using the 16-segment model. The colour indicates the coronary artery territories supplying the wall segments. Diagrams how the parasternal long-axis (PSLAX),apical four-chamber (AP4CH,corresponding to A1 in the following figure), apical two-chamber (AP2CH, corresponding toA2) and parasternal short-axis(PSSAX) views. The left ventricular long axis is divided at three levels: apical(a), mid-papillary (m) and basal (b). Somesegments are visualized in more than one view (see numbers). In the analysis the motion pattern of the 16 segments is given a wall motion score: normal, hypokinetic (<25% inward motion),akinetic (25% motion) and dyskinetic(outward motion). a, anterior; as,anteroseptal; al, anterolateral; l, lateral;p, posterior; ps, posteroseptal; pl,posterolateral; pm, posteromedial; s, septal.

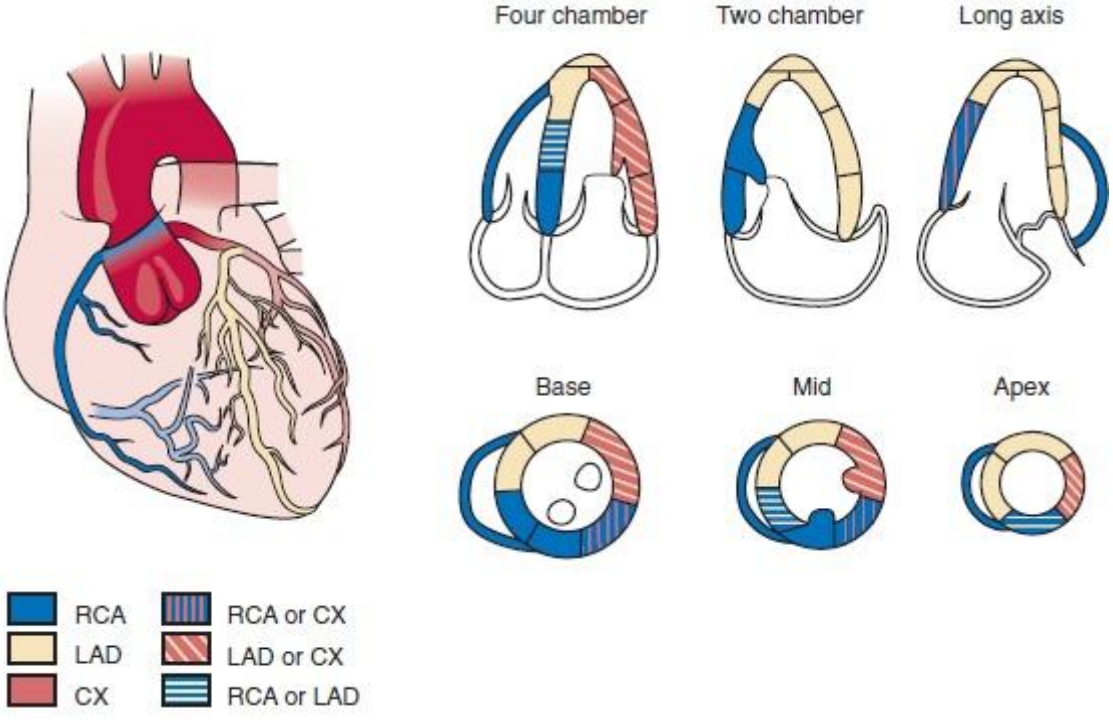




Method for standardized qualitative wall motion analysis using the 17-segment model



Segment level	AS	Ant	Ant Lat	Post Lat	Inf	IS
Basal	1	2	3	4	5	6
Mid	7	8	9	10	11	12
Apical	13	14	15	–	16	13



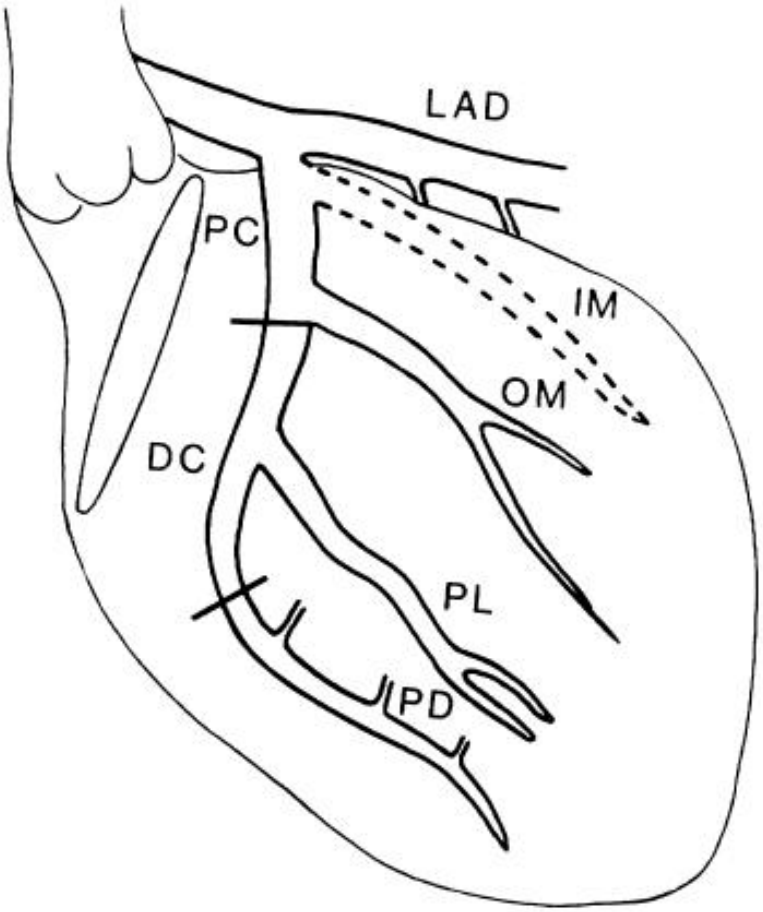
Coronary angiography

This is the gold standard to prove or exclude coronary artery disease. In approximately 10–15% of patients presenting with chest pain no high-grade lesion can be identified, or coronary artery disease is excluded. The extent and location of lesions is useful for risk assessment and decision-making concerning revascularization by means of angioplasty or surgery. The culprit lesions that are responsible for the clinical symptoms frequently show filling defects indicating intracoronary thrombus formation.

Left coronary artery cannulation

In the majority of cases a standard 4.0 Judkins catheter can be used. Occasionally, in small females a 3.5-mm or even 3.0-mm left Judkins catheter can be used as first choice; if it is known by previous invasive or noninvasive examination that there is an enlarged ascending aorta, a 4.5 or 5.0 left Judkins catheter can be preferred. The left coronary artery requires only minimal catheter manipulation.

Left circumflex coronary artery and its branches

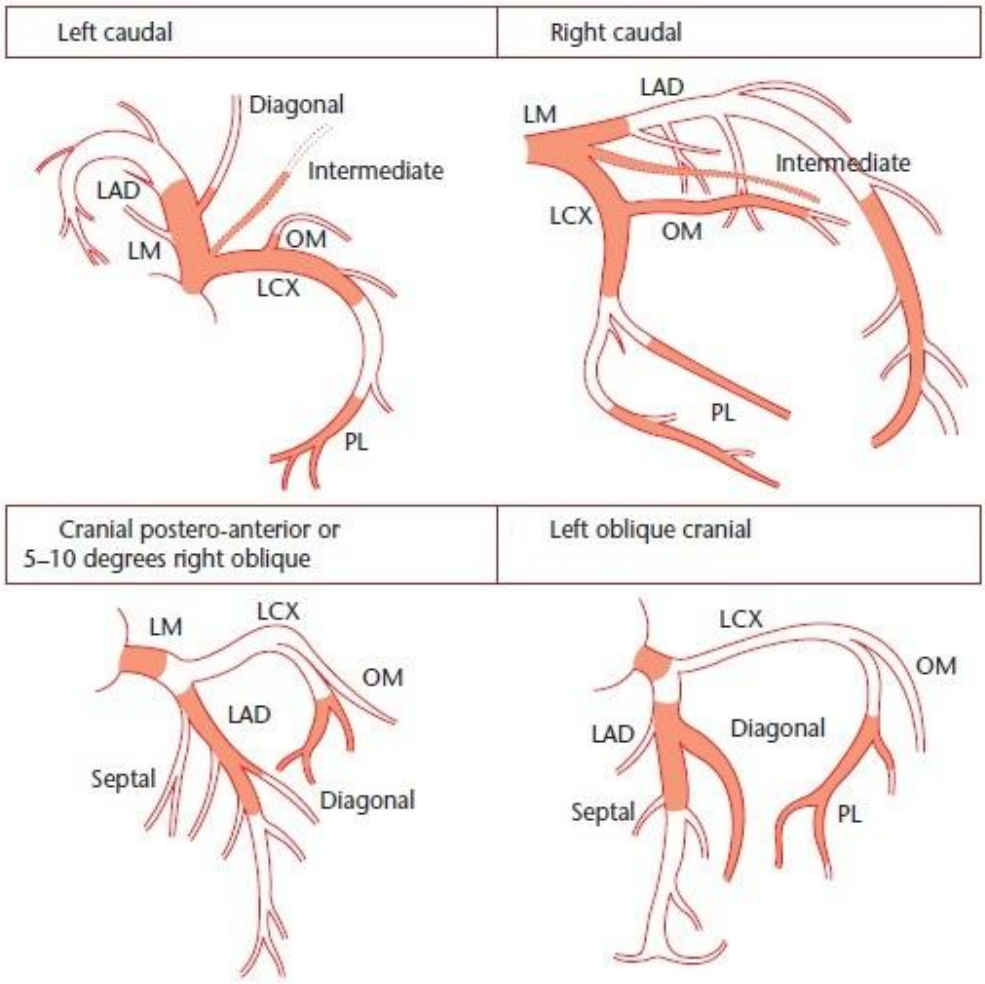


LAD – Left anterior descending coronary artery; PC – Proximal circumflex; DC – Distal circumflex; OM – Obtuse marginal; PL – Posterolateral branch; PD – Posterior descending artery.

Optimal views for left coronary circulation

The main advantage of the so-called spider view (left 40–55°, caudal 25–40°) is to delineate the branching of the left main coronary artery from the aorta and its bifurcation into the left anterior descending (LAD) and left circumflex (LCX) arteries (or trifurcation if an intermediate artery is present). The LAD artery is greatly foreshortened in the mid and distal segments in this view but stenosis of the proximal segment or of the ostium of the first diagonal branch is often optimally shown. The LCX artery, on the other hand, is optimally opened in its proximal and mid segments. The classical 30–40° right view is limited by the frequent superimposition of the proximal LAD and LCX and should be replaced by shallow right caudal views, which also offer less movement during respiration for angioplasty and which minimize irradiation. A smaller angulation to the right (10–20°) avoids superimposition of the catheter and the spine and, combined with relatively skewed caudal angulations(30–40°), opens the angle between LAD and LCX (and intermediate branch, if present) sufficiently to obtain optimal images of the proximal and mid segment of the LCX and bifurcation of its marginal branches. The image is of more limited interest for the proximal and mid LAD because of the frequent superimposition of diagonal and septal branches but remains the most important view for the distal LAD. Skewed cranial views (40° or more), with 5–10° angulation to the right to avoid superimposition of the

catheter and the vertebral spine, elongate the proximal and mid LAD and open the bifurcation of the proximal diagonal branches which run to the right, clearly distinguished from the septal branches which run to the left of the screen. The segments that are foreshortened in this view are the distal LAD and the proximal LCX but this view is also ideal for visualizing the distal poster lateral branches of the LCX and, in the 15–20%of cases with left dominance or codominance, the left posterior descending artery (PDA). In the left cranial view (30–45° left, 25–40° cranial) the LAD is further elongated by asking the patient to take a deep breath and maintain breath-holding during injection. The cranial view also offers optimal views of the mid and distal segments of the LCX, and is especially useful in the presence of a dominant LCX. The lateral view is far from standard in modern coronary angiography because the additional value of this view is quite limited, only providing excellent visualization of the mid/distal LAD around the apex, information which is at most complementary to right caudal views. Occasionally, however, eccentric short lesions of the proximal and mid segment of the LAD might be covered by septal or diagonal branches in all the conventional previously reported views and can be better visualized in the lateral projection, sometimes using variable cranial or caudal angulations to ensure no superimposition from the diagnostic catheter and side branches.



Optimal angiographic views for left circumflex coronary artery

Coronary Segment	**Origin/Bifurcation**	**Course/Body**
Proximal circumflex	RAO caudal	LAO caudal
	LAO caudal	
Intermediate	RAO caudal	RAO caudal
	LAO caudal	Lateral
Obtuse marginal	RAO caudal	RAO caudal
	LAO caudal	
	RAO cranial (distal marginal)	

MATERIALS AND METHODS

This study was conducted in the department of cardiology, Rajiv Gandhi Government General Hospital, Chennai during the year 2009 - 2012. This study is a retrospective study involving 55 patients.

Study group selection

Institutional ethics committee clearance was obtained to conduct this study in our hospital. All subjects provided written informed consent in the language known to participate in the study.

INCLUSION CRITERIA

Patients whose coronary angiogram showed isolated left circumflex coronary artery disease.

EXCLUSION CRITERIA

1) Patients with multi vessel coronary artery disease.
2) Patients with left anterior descending coronary artery disease.
3) Patients with right coronary artery disease.
4) Patients with advanced heart failure
5) Chronic kidney disease
6) Resting oxygen saturation less than 90%

Baseline characteristics of patients

1724 angiograms done over a period of 2 years were screened for study. Only 55 patients who fulfilled the eligibility criteria were included in the study. Out of 55 patients selected for the study, 50 were male(91%) and 5 were female(9%). Mean age of the study population was 52.5 years. Range (34 – 70 years).

Out of 55 patients, 35 patients (64%) underwent diagnostic coronary angiogram for documented myocardial infarction. Remaining 20 patients (36%) had angina on effort as the indication for coronary angiogram.

In patients whose coronary angiogram showed isolated left coronary circumflex artery disease following parameters were studied

1) Mode of clinical presentation (UA, NSTEMI, STEMI)
2) Electrocardiographic findings and their distribution and pattern in various leads
3) Echocardiographic analysis with respect to regional wall motion abnormalities, ejection fraction and presence of MR
4) Coronary angiogram analysis with respect to number, severity and distribution of stenosis.
5) Risk factor analysis.

Clinical presentation

The mode of clinical presentation of the study population was assessed with respect to presentation as effort angina, unstable angina, NSTEMI and STEMI. Rhythm disturbance during acute presentation as STEMI was also assessed. Hemodynamic parameters was specifically looked for in patients presented with STEMI.

Electrocardiographic findings

ECGs of the study population was scrutinised with respect to presence or absence of Q waves, presence or absence of ischemic ST- T changes. The location and magnitude of ST-T changes were also analysed. Combination of Q waves and ST-T changes were specifically looked for especially in patients presented with STEMI. The location of ECG changes with respect to leads were analysed. These ECG changes were then correlated with the location of the lesion in LCX. Patterns of high lateral MI and RV MI were also analysed. Posterior MI was assessed by posterior leads in addition to standard ECG leads. RVMI was assessed by right sided chest leads in addition to standard chest leads. The pattern of ECG changes with respect to various location of stenosis in LCX was also studied. Other associated features such as LBBB, RBBB and LVH were also analysed.

Echocardiographic analysis

Baseline LV systolic function was assessed by modified Simpsons's method in all study patients. LV dysfunction was characterised as mild if the LV ejection fraction was between 46 – 55%. Moderate LV dysfunction was defined as LV ejection fraction between 30 – 45%. Severe LV dysfunction was defined as LV EF less than 30%. Normal LV function was defined as LV EF above 55%.

All the study population underwent colour flow imaging for the presence of mitral regurgitation. Mitral regurgitation was graded as mild, moderate and severe as per AHA guidelines.

Regional wall motion abnormality was assessed for patients presented with documented STEMI.

Angiographic analysis

The diagnostic coronary angiograms of the study population was collected and assessed. The location and severity of stenosis in LCx was studied in detail in multiple angiographic views. The number of stenosis in LCX was also analysed. Significant stenosis was defined as stenosis more than or equal to 70% in LAD, LCX and RCA. Significant stenosis in LMCA was defined as stenosis severity more than or equal to 50%.

Presence of nonsignificant stenosis in RCA and LAD (stenosis severity less than 50%) were also studied. Nonsignificant stenosis in LMCA was defined as stenosis severity less than 30%. The dominance of the coronary artery was assessed.

For the sack of analysis, LCX was divided into proximal and disal segments. The portion of LCX above the origin of OM1 was considered proximal. The distal segment was defined as portion of LCX below the origin of OM1. Presence of stenosis in OMs was specifically looked for in patients presented with high lateral MI.

Collateral circulation was also assessed in patients showing total or near total occlusion of LCX.

Risk factor analysis

The study population was assessed for the presence of major risk factors for CAD. These include hypertension, diabetes mellitus, family history of coronary artery disease, smoking and hypercholesterolemia. The average risk factor per patient was then calculated. The number of risk factors in patient population was also assessed with respect to single, multiple or no risk factor.

RESULTS & DATA ANALYSIS

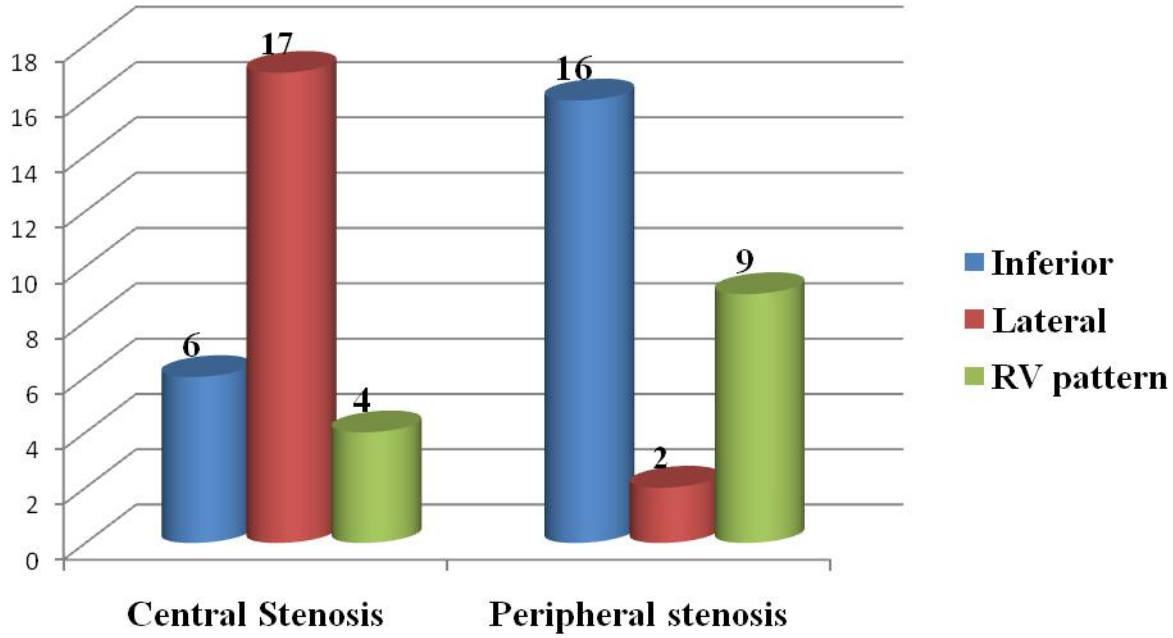
Statistical analysis was carried out for 55 patients who fulfilled both inclusion and exclusion criteria after categorising each variable. Age, Sex, Indication for coronary angiogram, ECG abnormalities, Distribution of stenosis, LV function and risk factors were analysed.

Indication for coronary angiogram was documented myocardial infarction in 35 patients (64%) among the study population. Angina pectoris on effort was the indication for coronary angiogram in 20 patients (36%) among the study population.

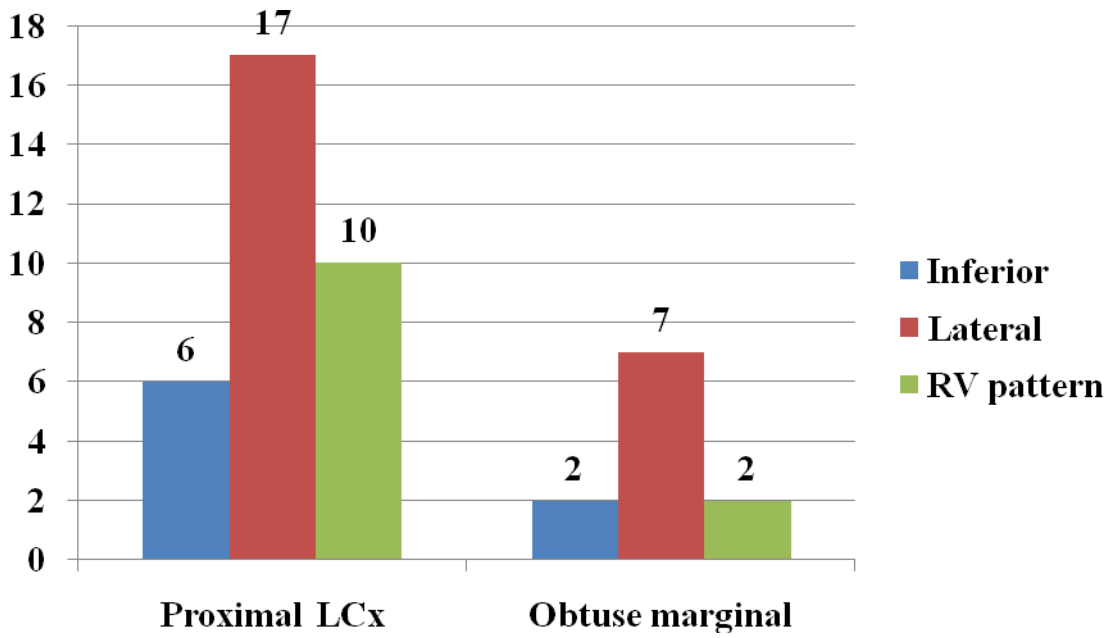
30 patients (54.5%) showed Q waves in the resting ECG. Q waves were seen in inferior leads in 20 patients, lateral leads in 6 patients and both in inferior and lateral leads in 4 patients. Ischemic ST-T changes were noted in 40 patients (72%). Ischemic ST-T changes were seen in inferior leads in 28 patients, lateral leads in 7 patients and both in inferior and lateral leads in 5 patients. RV pattern of ECG changes was noted in 15 patients (27.3%) among the study population. RV pattern was noted in inferior leads in 14 patients and both in inferior and lateral leads in 1 patient. In the resting ECG, 12 patients (21.8%) had normal ECG. LBBB was noted in 1 patient (2%) of study population. RBBB was noted in 3

patients (5.4%). LVH was noted in 7 patients (12.7%). 27 patients (49%) showed both Q waves and ischemic ST-T changes in their resting ECG. 13 patients (23.6%) showed only ischemic ST-T changes in the resting ECG.

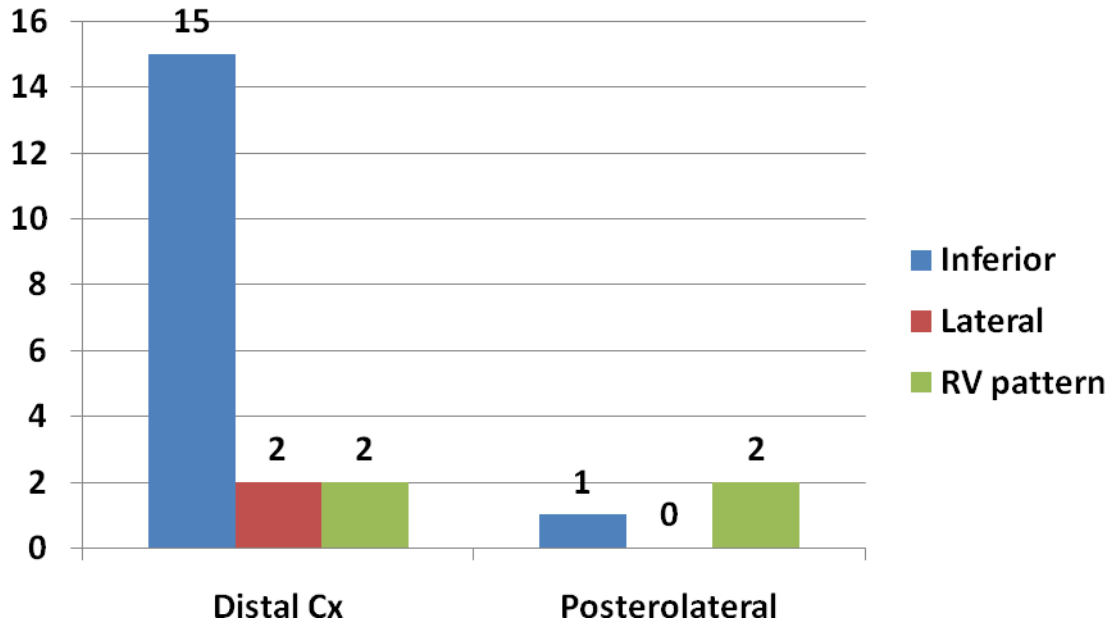
Inferior and lateral patterns of ECG abnormalities in patients with solitary stenoses in segments of the left circumflex coronary artery



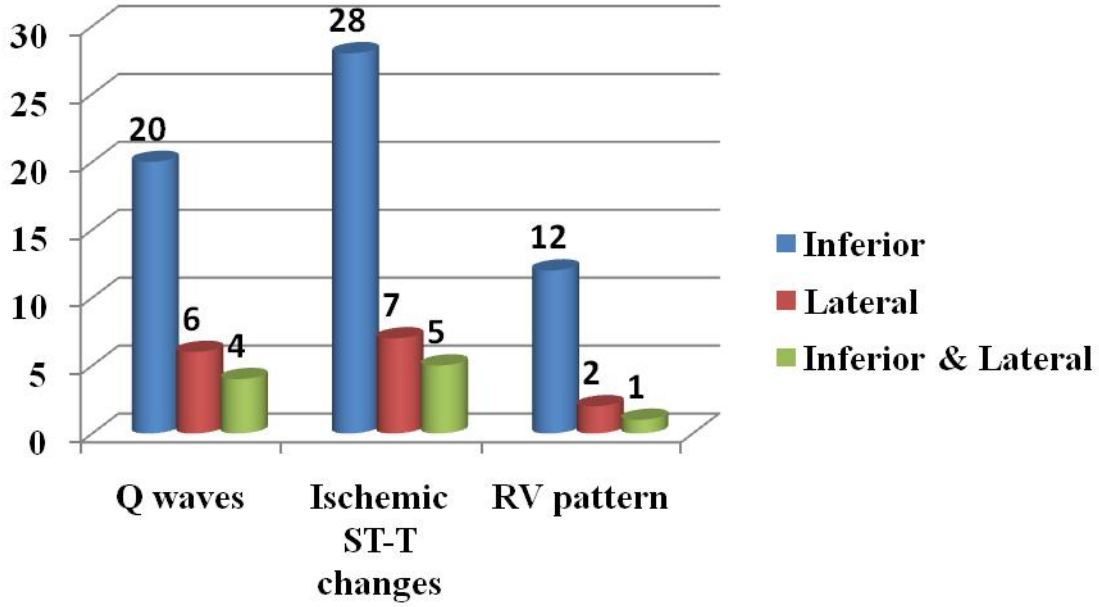
ECG abnormalities in patients with single stenosis centrally



ECG abnormalities in patients with single stenosis peripherally



ECG CHANGES WITH RESPECT TO LEADS

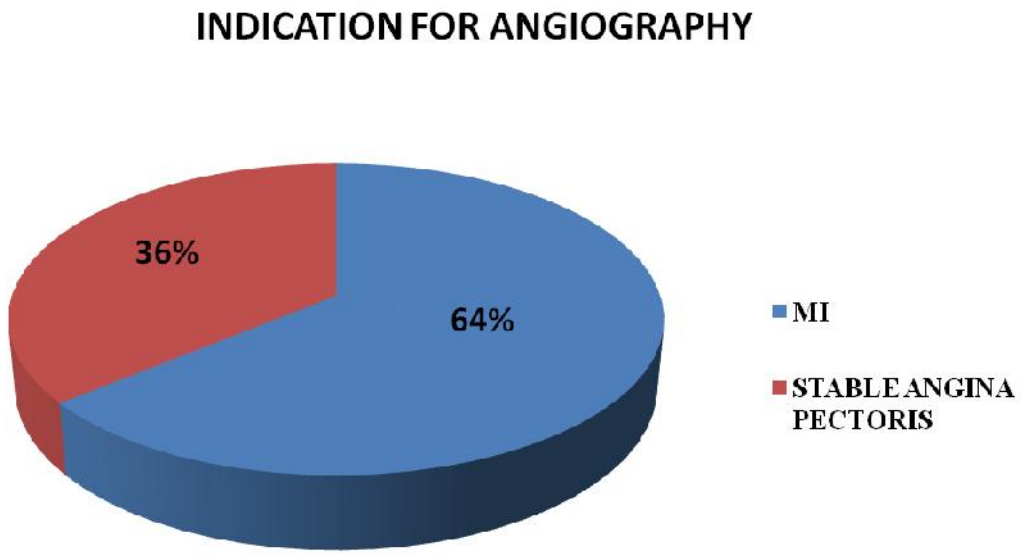


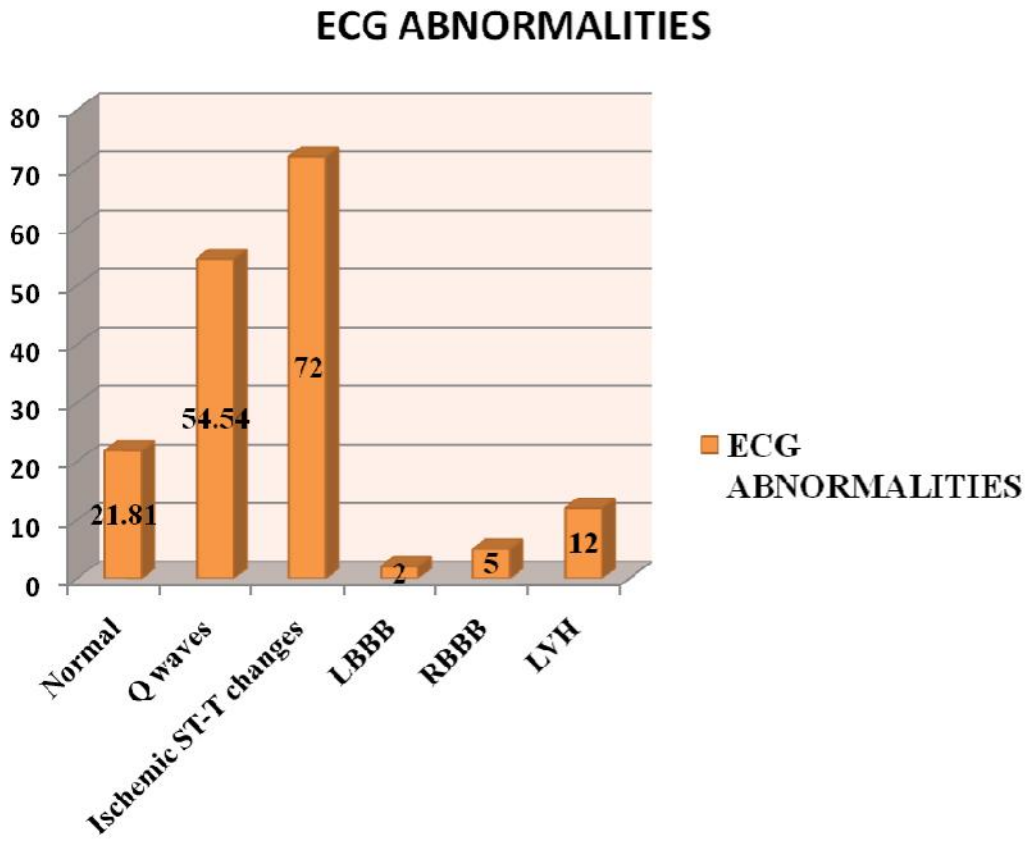
41 patients (74.5%) among the study population had positive tread mill test. Out of 41 patients, 21 had documented evidence of myocardial infarction. Rest of the 20 patients underwent TMT for angina pectoris for effort. Tread mill test was not done in the rest of the study population (14 patients, 25.5%).

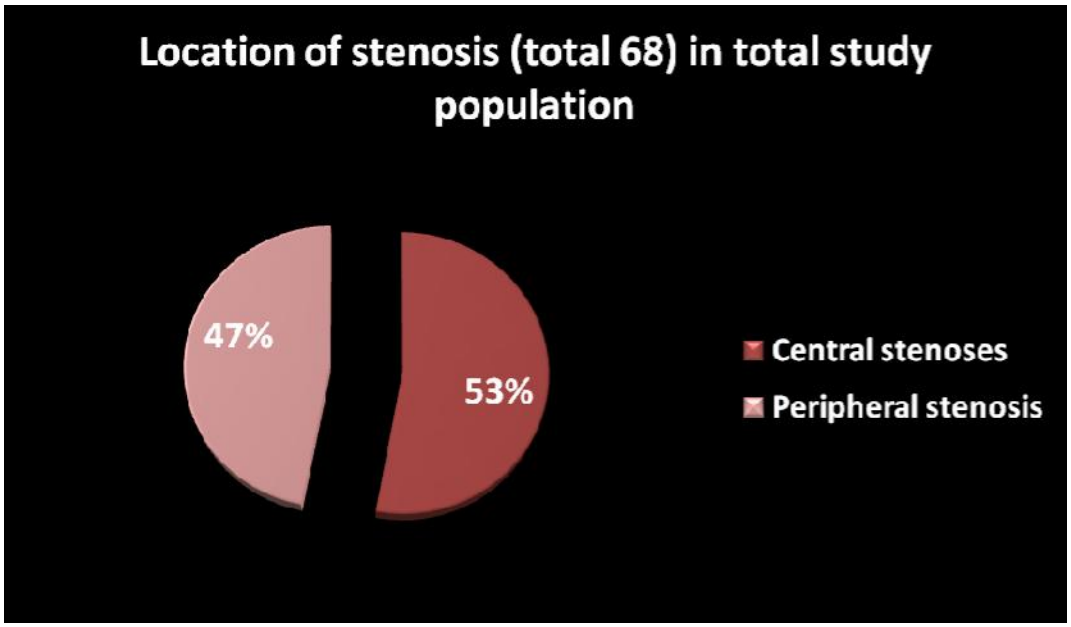
Total number of stenosis noted in left circumflex coronary artery and its branches among the study population was 68. Out of 68 stenosis, 36 (53%) were central and 32 (47%) were periphery. The distribution of central stenosis was proximal LCx 20 (29%), obtuse marginal branches 14

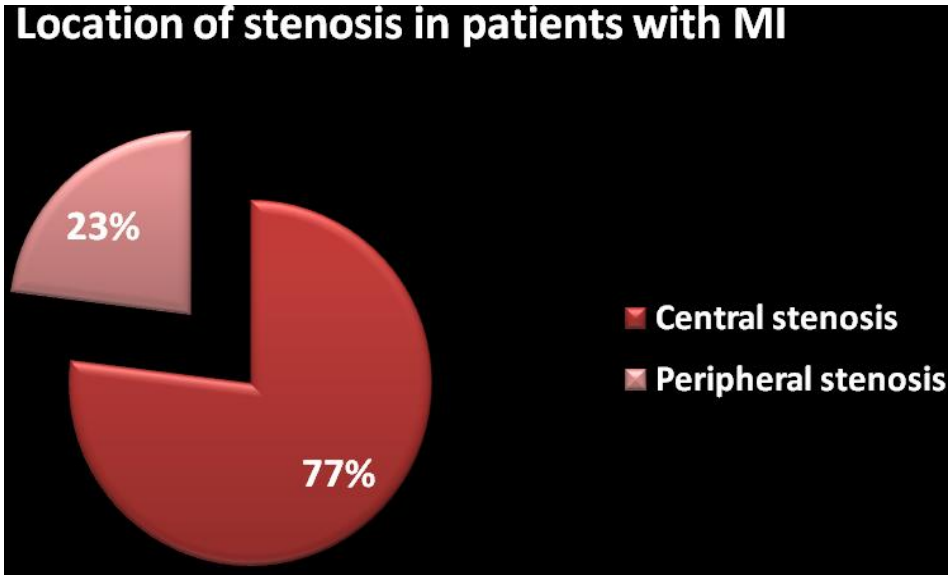
(21%), intermediate 2 (3%). The distribution of peripheral stenosis was distal LCx 30 (44%) and Posterolateral branches 2 (3%).

Single stenosis in left circumflex coronary artery and its branches was seen in 43 patients (78%) among the study population. 11 patients (20%) showed double stenosis. Triple stenosis was noted in one patient (2%).

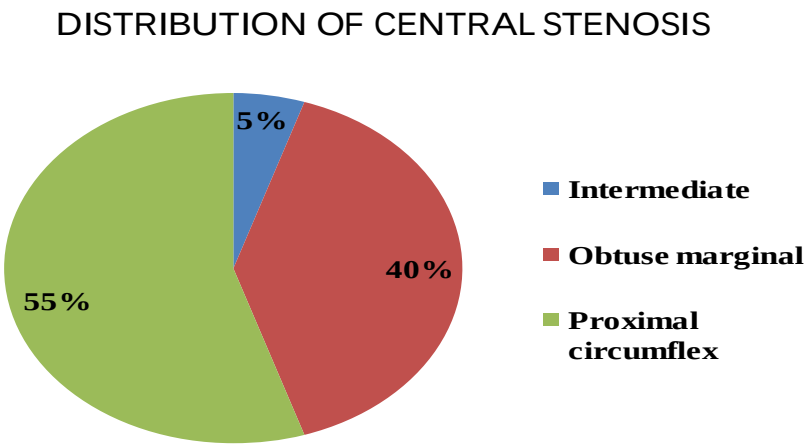


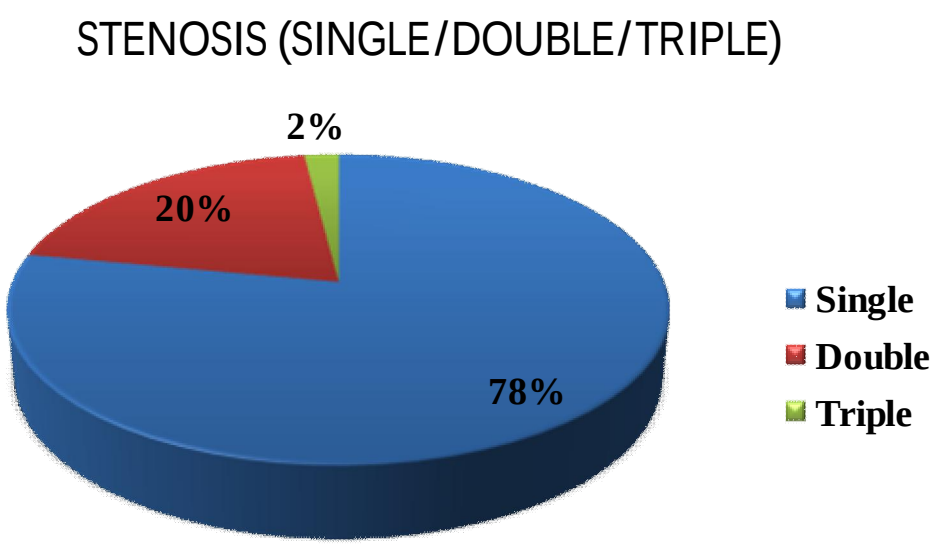

ECG ABNORMALITIES
80
70
60
50
40
30
20
10
0
21.81
54.54
72
2
5
12
Normal
Q waves
Ischemic ST-T changes
LBBB
RBBB
LVH
ECG ABNORMALITIES


Location of stenosis (total 68) in total study population
47%
53%
Central stenoses
Peripheral stenosis


Location of stenosis in patients with MI
23%
77%
Central stenosis
Peripheral stenosis

43 patients (78%) among the study population showed single stenosis in left circumflex coronary artery and its branches. Out of 43 stenosis 23 were central and 20 were peripheral. Out of 23 central stenosis 13 were noted in proximal left circumflex coronary artery and 10 were noted in obtuse marginal branches. Out of 20 peripheral stenosis, 19 stenosis were noted in distal LCx and 1 in Posterolateral branches.

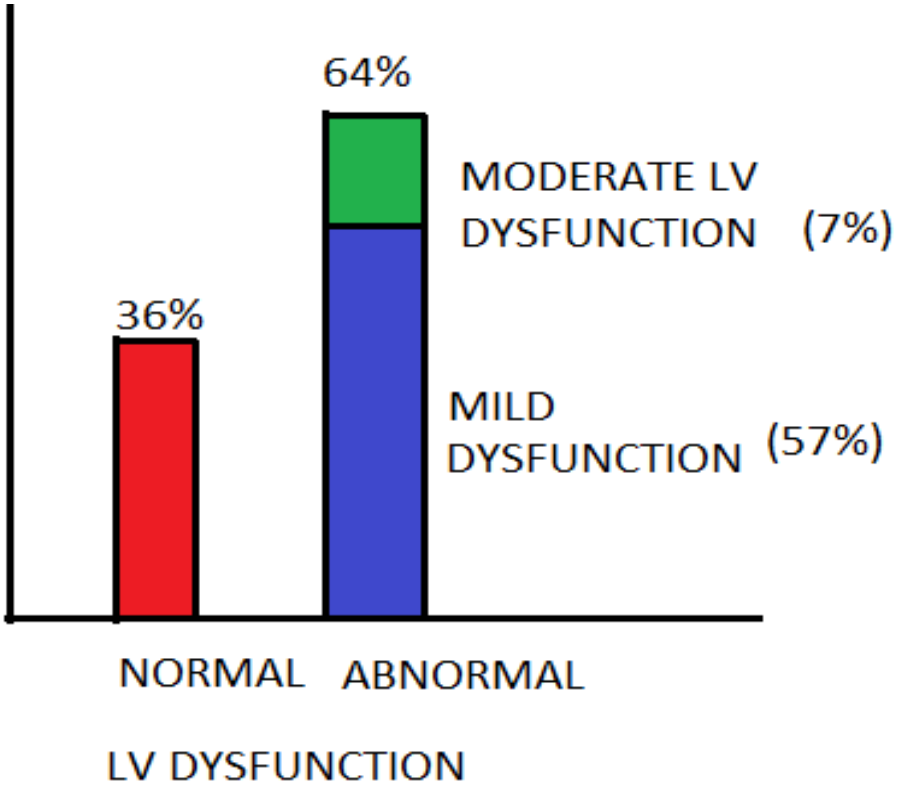




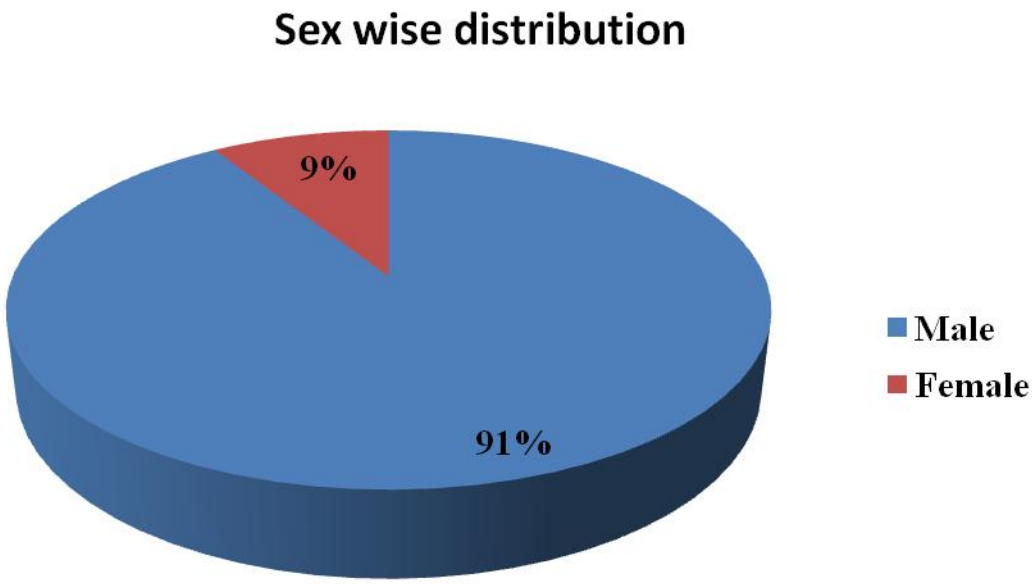
Non significant stenosis (<70%) in left anterior descending artery was noted in 22 patients(40%) among the study population. Non significant stenosis in right coronary patients was noted in 16 patients (29%). Non significant stenosis (<50%) in left main coronary artery was noted in 1 patient (1.8%) among the study population.

Left ventricular ejection fraction (EF) was calculated by modified Simpson's method. Mean ejection fraction of study group was 53.16%. 20 patients (36%) among the study population had normal EF (>55%). 35 patients (64%) had reduced ejection fraction. Mild LV dysfunction (EF 46-55%) was noted in 31 patients (57%) among the study population. Moderate LV dysfunction (EF 30-45%) was noted in 4 patients (7%).

None among the study population had severe LV dysfunction (EF <30%). Mild mitral regurgitation was noted 4 patients (7.2%) among the study population. Those patients who showed mild mitral regurgitation had moderate LV dysfunction and had evidence of documented MI.



Out of 55 study population, 50 were male (91%) and 5 were female (9%).



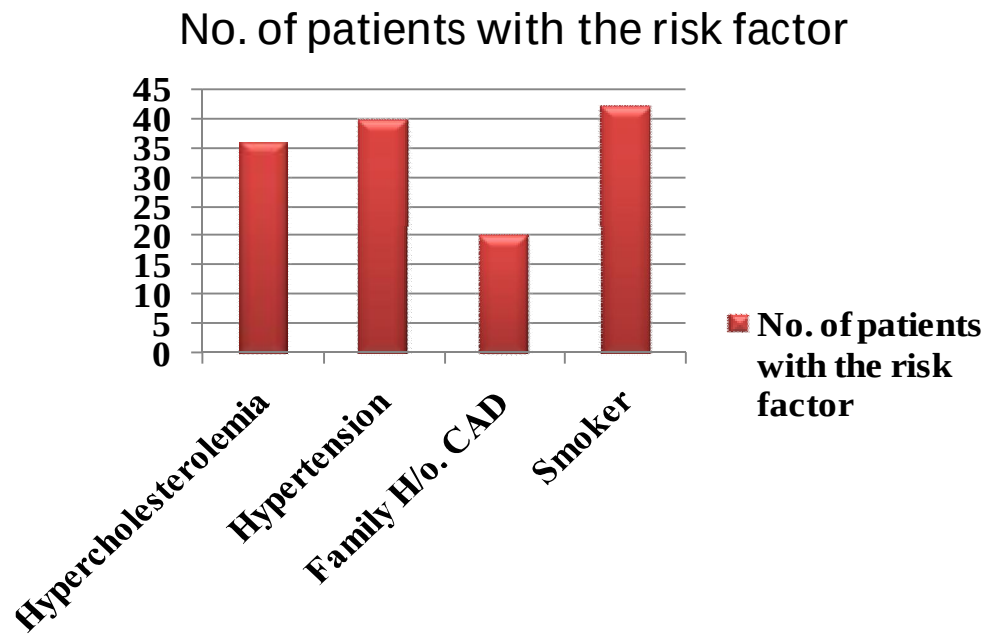
40 patients (72.7%) among the study population had hypertension. 42 patients (76.3%) were smokers. Hypercholesterolemia were noted in 36 patients (65.4%). Family history of coronary artery disease was obtained in 20 patients (36.6%). 20 patients had type 2 diabetes mellitus (36.4%). Average risk factor is 2.8 per patient. Number of patients with no risk factor is 2 (4%), single risk factor is 5 (9%) and those with multiple risk factors is 48 (87%).

INFERIOR AND LATERAL PATTERNS OF ECG ABNORMALITIES IN PATIENTS WITHSOLITARY STENOSES IN SEGMENTS OF THE LEFT CIRCUMFLEX CORONARY ARTERY

Location of stenosis	No. of patients	ECG Pattern		
		Inferior	Lateral	RV pattern
Central	23	6	17	4
Proximal LCx	13	4	10	2
Obtuse marginal	10	2	7	2
Intermediate	0	0	0	0
Peripheral	20	16	2	9
Distal LCx	19	15	2	9
Posterolateral	1	1	0	0
Total	43	22	19	13

DISTRIBUTION OF STENOSIS

Site of Stenosis	No. of Stenosis	% of total
Central	36	53
Proximal LCx	20	29
Obtuse marginal	14	21
Intermediate	2	3
Peripheral	32	47
Distal Cx	30	44
Posterolateral	2	3



ECG CHANGES WITH RESPECT TO LEADS

	Electrocardiographic changes			
	Total	**Inferior**	**Lateral**	**Inferior & Lateral**
Q waves	30	20	6	4
Ischemic ST-T changes	40	28	7	5
RV pattern	15	14	0	1
LBBB	1	-	-	-
RBBB	3	-	-	-
LVH	6	-	-	-

DISCUSSION

Isolated left circumflex coronary disease is infrequently shown at angiography. The prevalence of isolated left circumflex disease in this study is 3.2%. Majority of the patients in this study had documented evidence of myocardial infarction and underwent coronary angiogram as a result of higher risk stratification scores. This may have accounted for the lower incidence of TMT positive effort angina in the study population. Isolated disease of the left circumflex coronary artery does not appear to cause severe left ventricular dysfunction, as the mean ejection fraction in our patients was 53.16% and this is in accord with previous reports[1].

Electrocardiographic abnormalities occurred in the inferolateral leads (inferior pattern in leads II, III, aVF, V5. and V6,) anterolateral leads (lateral pattern in leads I, aVL, V5, and V6), and right precordial leads (RV pattern in leads V1 and V2) in patients with solitary stenosis of left circumflex coronary artery disease. The lateral pattern and RV pattern are more specific for circumflex disease[4]. Left circumflex coronary artery was basically divided into proximal and distal segments to determine whether these more specific patterns of ECG changes correlated with disease in specific segments of the circumflex coronary artery. Inferior electrocardiographic changes can also occur in patients with isolated right

coronary artery disease and are not specific for left circumflex coronary artery disease.

Gensini et al[40] suggested that most stenoses are proximal. In our study also, the sites of stenoses reflect the sites of predilection for atherosclerosis in patients with isolated circumflex disease and include proximal and distal circumflex segments and proximal portions of the major branches. The portions of the branches of circumflex coronary artery beyond the major bifurcation were usually free of segmental stenosis[33].

In contrast to the findings of Gensini et al[40], no ostial or ostioproximal lesion involving left circumflex coronary artery were noted in our study.

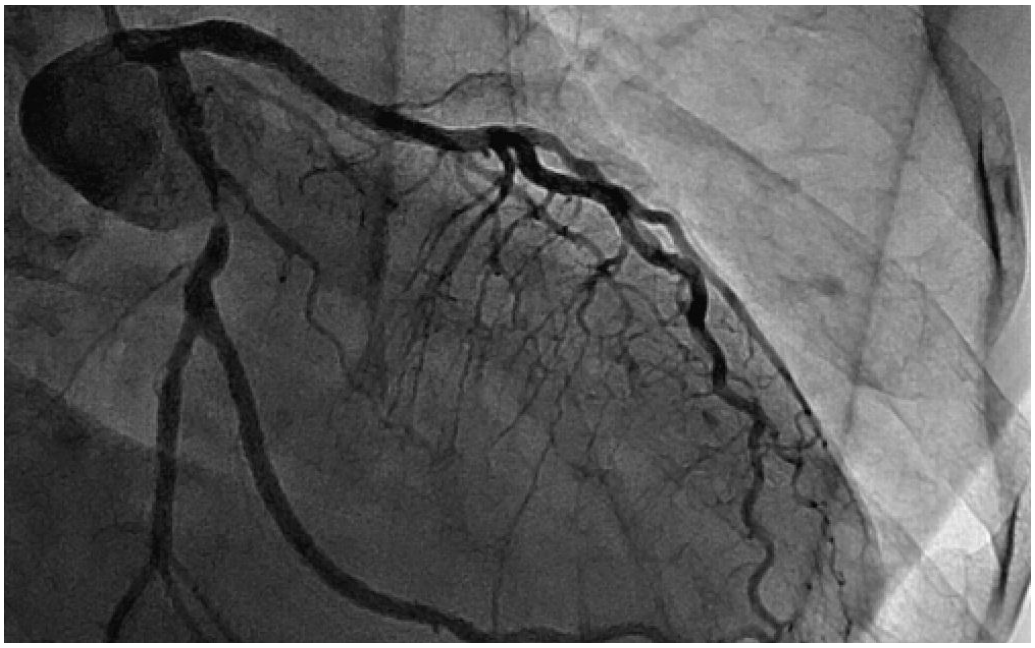
Relation Between ECG Patterns and LCx Stenosis

The electrocardiographic data were based on information obtained from 43 patients with solitary stenosis in the circumflex coronary artery[32] so that the patterns of electrocardiographic abnormalities could be related to stenosis inindividual segments of the circumflex coronary artery. A stenosis in the obtuse marginal branch of the circumflex was associated with the lateral pattern of electrocardiographic abnormalities.This is predictable because the obtuse marginal branch of the circumflex usually supplies the posterolateral myocardium. Disease in the proximal segment

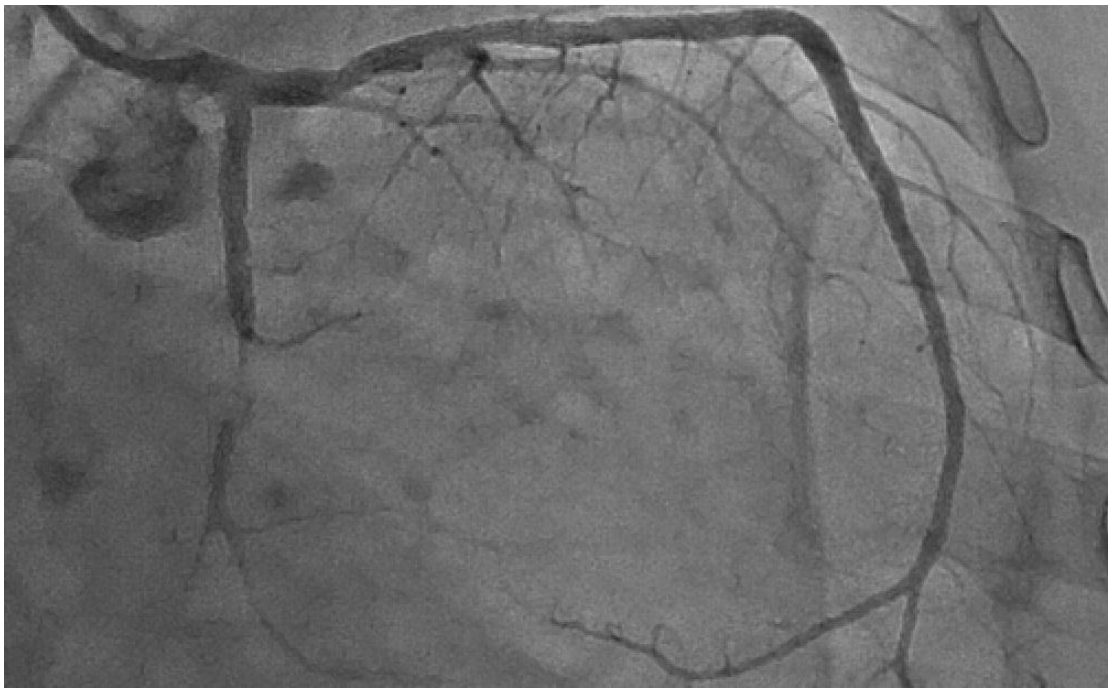
of the circumflex was predominantly associated with lateral electrocardiographic pattern. This association may reflect the fact that the proximal circumflex supplies both the posterolateral and posteroinferior myocardium. A peripheral stenosis distal to the takeoff of the obtuse marginal branch was predominatly associated with the inferior pattern of electrocardiographic abnormalities. This is consistent with the fact that the distal circumflex supplies blood to the posteroinferior myocardium. The posterolateral branch contributes to the blood supply of the posterior myocardium, and stenosis of the posterolateral branch is associated with inferior electrocardiographic changes.

Braat et al[44] have shown that the recording of lead V4R in the acute phase of an inferior myocardial infarction may be useful in predicting coronary artery occlusion. Patients with ST-segment elevation of >l mm in lead V4R often had a proximal occlusion of the right coronary artery and those who had no ST-segment elevation in lead V4R developed a distal occluded right coronary artery. Negative T wave in lead V4R is associated with occlusion of left circumflex coronary artery disease.ST-segment elevation of >1 mm in leads aVL and lead I predicted a circumflex artery occ1usion.

CAG 90% stenosis in LCx just after the origin of OM1



CAG showing 99% long segment stenosis of intermediate segment of LCx



CAG showing ostio proximal stenosis at the origin of OM1

The incidence of an abnormal R wave in lead V1 occurred more frequently in patients with proximal stenosis than in those with distal lesion of the LCx. An abnormal R wave in lead V1was often associated with inferior and/or lateral Q waves, reflecting thefact that the proximal LCx supplies both posterolateral and posteroinferior myocardium, and a single occlusion in such a vessel could readily cause simultaneous infarction of the lateral and inferior walls. Brembilla-Parrot et al[42]found that in some patients a tall R wave in lead V1**,** during posterior myocardial infarction may also be caused by conduction disturbance in the His-Purkinje system rather than just mirroring loss of activation forces at the posterolateral region.

Only 4 patients among the study population had mitral regurgitation. Mitral regurgitation occurred in patients with LV dysfunction. This correlates with the observation that most of the patients with isolated left circumflex coronary artery disease have normal left ventricular function.

Clinical implications

Isolated circumflex disease may be suspected by applying the clinical and electrocardiographic criteria, but cannot be definitely diagnosed. The left ventricular function is patients with isolated left circumflex coronary artery disease is relatively preserved. Most of the patients have normal ejection fraction and normal left ventricular function.

CONCLUSIONS

- Incidence of isolated left circumflex coronary artery disease is 3.2%.
- Single stenosis is the most common finding in the coronary angiogram of the patients with isolated LCX disease.
- Central stenosis involving proximal left circumflex coronary artery is more common than peripheral stenosis involving distal LCX.
- Central stenosis involving proximal LCX is more common in patients with documented evidence of MI.
- Most of the patients with isolated LCX disease have normal left ventricular function.
- ECG changes in lateral leads are common is patients with stenosis in proximal LCX.
- ECG changes in inferior leads are common in patients with stenosis in distal LCX.
- Average risk factor per patient is 2.8%.

CLINICAL, ELECTROCARDIOGRAPHIC, ECHOCARDIOGRAPHIC AND ANGIOGRAPHIC PROFILE OF ISOLATED LEFT CIRCUMFLEX CORONARY ARTERY DISEASE

PROFORMA

Serial No.:

Initials:

Age:

Sex: Male – 1 Female – 2

Diagnosis:

CD No.:

Occupation:

Address:

RISK FACTORS:

Hypercholesterolemia Yes – 1 No – 2

SHT Yes – 1 No – 2

Smoking Yes – 1 No – 2

Family H/o. CAD Yes – 1 No – 2

DM Yes – 1 No – 2

CLINICAL FEATURES:

Effort Angina Yes – 1 No – 2

TMT Positive – 1 Negative – 2 Not done – 3

Documented MI Yes – 1 No – 2

ECG

Q waves Present – 1 Absent – 2

ST-T changes Present – 1 Absent – 2

Lateral wall changes Present – 1 Absent – 2

Inferior wall changes Present – 1 Absent – 2

Inferior & lateral wall changes Present – 1 Absent – 2

ECHO

LVEF :

MR Present – 1 Absent – 2

RWMA Present – 1 Absent – 2

LV dysfunction Present – 1 Absent – 2

CAG

Proximal LCX stenosis Present – 1 Absent – 2

Distal LCX stenosis Present – 1 Absent – 2

OM1 stenosis Present – 1 Absent – 2

RCA stenosis Present – 1 Absent – 2

LAD stenosis Present – 1 Absent – 2

LCX Nondominant – 1 Dominant – 2

CAG - NO. OF STENOSIS IN LCX

Single – 1 Double – 2 Triple – 3

Sl. No.	AGE	SEX	RISK FACTORS					CLINICAL FEATURES			ECG					ECHO			CAG - Location of stenosis					CAG-NO OF STENOSIS IN LCX
			SHT	HYPER CHOLESTEROLEMIA	SMOKING	FAMILY H/O. CAD	DM	EFFORT ANGINA	TMT	DOCUMENTED MI	Q WAVES	ST-T CHANGES	LATERAL WALL CHANGES	INFERIOR WALL CHANGES	INFERIOR WALL CHANGES	LVEF (%)	MR	LV DYSFUNCTION	PROXIMAL LCX	OM BRANCHES	INTERMEDIATE	DISTAL LCX	POSTEROLATERAL	
1	48	1	1	1	1	2	2	2	3	1	1	2	1	2	2	58	2	2	1	2	2	2	2	1
2	34	1	1	1	2	2	2	1	1	2	2	1	2	2	1	50	2	1	2	2	2	1	2	1
3	57	1	1	2	1	1	2	2	3	1	1	1	1	2	2	60	2	2	2	1	2	1	2	2
4	40	1	1	1	1	2	2	1	1	2	2	2	2	2	2	47	2	1	2	2	2	1	2	1
5	44	1	2	2	1	1	1	2	1	1	1	1	2	1	2	52	2	1	1	1	2	1	2	2
6	60	2	1	2	2	2	2	1	1	2	2	2	2	2	2	60	2	2	2	2	2	1	2	1
7	45	1	2	1	1	1	2	2	3	1	1	1	2	1	2	50	1	1	1	2	2	2	2	1
8	56	1	1	1	1	2	2	1	1	2	2	2	2	2	2	62	2	2	2	2	2	1	2	1
9	60	1	1	1	1	1	2	2	3	1	1	1	2	1	2	40	2	1	1	2	2	1	2	2
10	55	1	1	1	1	1	1	2	1	1	1	1	1	2	2	48	2	1	1	2	2	2	2	1
11	60	1	1	1	2	1	2	1	1	2	2	2	2	2	2	56	2	2	2	1	2	1	2	2
12	52	2	1	2	2	2	2	2	1	1	1	1	2	1	2	50	2	1	2	1	2	2	2	1
13	54	1	1	2	1	1	2	2	3	1	1	1	2	1	2	52	2	1	1	2	2	2	2	1
14	40	1	1	1	1	2	1	2	1	1	2	1	2	1	2	48	2	1	1	2	2	2	2	1
15	53	1	1	2	1	1	2	2	1	1	1	2	2	1	2	58	2	2	1	2	2	2	2	1
16	60	1	1	1	1	2	1	2	1	1	1	1	2	1	2	50	2	1	1	1	2	2	2	2
17	51	1	1	1	1	1	2	2	3	1	1	1	2	1	2	60	2	2	1	2	2	2	2	1
18	58	1	1	2	1	2	2	1	1	2	2	1	2	2	1	48	2	1	2	2	2	1	2	1
19	51	1	2	1	1	1	2	2	1	1	1	1	2	2	1	50	2	1	1	2	1	2	2	2
20	48	1	2	2	1	2	2	2	1	1	2	1	2	1	2	53	2	1	1	2	2	2	2	1
21	46	1	2	2	1	2	1	1	1	2	2	2	2	2	2	60	2	2	2	2	2	1	2	1
22	61	1	2	1	2	1	2	2	3	1	1	1	2	1	2	52	2	1	1	2	2	2	2	1
23	59	1	1	1	1	2	1	2	1	1	1	1	2	2	1	51	2	1	1	1	2	2	2	2
24	57	2	2	2	1	2	1	2	3	1	2	1	2	1	2	58	2	2	2	1	2	2	2	1
25	70	1	1	2	2	2	2	2	3	1	1	1	2	2	1	52	2	1	1	2	2	2	2	1
26	67	1	1	2	1	1	1	1	1	2	2	2	2	2	2	58	2	1	2	2	2	1	2	1
27	39	1	1	1	2	2	2	2	1	1	1	1	2	1	2	46	2	1	2	1	2	2	2	1
28	43	2	1	1	1	2	1	1	1	2	2	2	2	2	2	68	2	2	2	2	2	1	2	1
29	47	1	2	1	1	2	2	2	1	1	1	1	2	1	2	51	2	1	1	2	2	2	2	1
30	62	1	1	1	1	2	2	2	1	1	1	1	2	1	2	44	1	1	2	1	2	2	2	1

Sl. No.	AGE	SEX	RISK FACTORS					CLINICAL FEATURES			ECG					ECHO			CAG - Location of stenosis					CAG-NO. OF STENOSIS IN LCX
			SHT	HYPER CHOLESTEROLEMIA	SMOKING	FAMILY H/O. CAD	DM	EFFORT ANGINA	TMT	DOCUMENTED MI	Q WAVES	ST-T CHANGES	LATERAL WALL CHANGES	INFERIOR WALL CHANGES	LATERAL & INFERIOR WALL CHANGES	LVEF (%)	MR	LV DYSFUNCTION	PROXIMAL LCX	OM BRANCHES	INTERMEDIATE	DISTAL CX	POSTEROLATERAL	
31	57	1	1	1	1	1	1	1	1	2	2	2	2	2	2	50	2	1	2	2	2	1	2	1
32	61	1	1	1	1	1	2	2	1	1	2	1	2	1	2	64	2	2	2	1	2	2	2	1
33	55	1	2	1	1	2	1	1	1	2	2	2	2	2	2	47	2	1	2	2	2	1	2	1
34	42	1	1	1	1	2	1	2	3	1	1	1	2	1	2	62	2	2	2	2	2	1	2	1
35	60	1	1	2	1	1	1	1	1	2	2	2	2	2	2	50	2	1	2	2	2	1	2	1
36	61	1	1	2	1	2	2	2	1	1	1	2	2	1	2	66	2	2	1	2	2	2	2	1
37	63	1	1	1	2	1	1	1	1	2	2	1	2	1	2	48	2	1	2	2	2	1	2	1
38	45	1	1	1	1	2	1	2	1	1	1	1	1	2	2	38	1	2	1	1	2	2	1	3
39	40	1	2	2	1	2	1	1	1	2	2	1	2	1	2	49	2	1	2	2	2	1	2	1
40	56	1	1	2	2	2	2	2	3	1	1	1	2	1	2	53	2	1	1	1	2	2	2	2
41	49	1	1	2	1	1	2	2	1	1	1	1	2	1	2	53	2	1	2	1	2	2	2	1
42	44	1	2	2	2	2	2	1	1	2	2	2	2	2	2	60	2	2	2	2	2	1	2	1
43	42	1	1	2	2	2	2	2	1	1	1	1	1	2	2	49	2	1	1	2	2	2	2	1
44	63	1	1	1	1	2	1	2	3	1	2	1	1	2	2	60	2	2	2	1	2	2	2	1
45	48	1	2	1	1	1	2	2	1	1	1	1	2	1	2	50	2	1	1	2	2	1	2	2
46	58	1	1	1	1	2	1	2	3	1	1	1	2	2	1	40	1	1	2	1	2	2	2	1
47	62	1	1	1	1	2	2	2	1	1	1	1	2	1	2	49	2	1	1	2	2	1	2	2
48	39	1	1	1	1	2	1	1	1	2	2	2	2	2	2	62	2	2	2	2	2	1	2	1
49	54	1	1	1	1	1	2	1	1	2	2	1	1	2	2	50	2	1	2	2	2	1	2	1
50	60	1	2	2	2	2	2	1	1	2	2	1	2	1	2	48	2	1	2	2	2	1	2	1
51	52	1	1	2	2	2	2	2	1	1	1	1	1	2	2	60	2	2	1	2	1	2	2	2
52	60	2	1	1	1	1	2	1	1	2	2	1	2	1	2	50	2	1	1	2	2	2	2	1
53	50	1	2	1	1	2	2	2	1	1	1	1	2	1	2	64	2	2	2	1	2	2	2	1
54	50	1	2	1	1	2	2	1	1	2	2	1	2	1	2	52	2	1	2	2	2	1	2	1
55	44	1	1	1	1	2	2	2	3	1	1	1	2	1	2	58	2	2	2	2	2	2	1	1

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Shankar. P
PG in DM Cardiology
Madras Medical College, Chennai -3

Dear Dr. Shankar. P

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled " Clinical, electrocardiographic, echocardiographic and angiographic profile of isolated left circumflex coronary artery disease" No.37012012.

The following members of Ethics Committee were present in the meeting held on 27.01.2012 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan. MD	-- Chairperson
2	Prof. Pregna B. Dolia MD Vice Principal, Madras Medical College, Chennai -3 (Director , Institute of Biochemistry, MMC, Ch-3)	-- Member Secretary
3.	Prof. B. Kalaiselvi. MD Prof of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. Shruti Kamal MS Prof of Surgery, Madras Medical College , Ch-3	-- Member
5.	Thiru. S. Govindsamy. BA BL	-- Lawyer

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

ABBREVIATIONS

CXR	-	Chest X Ray
DM	-	Diabetes Mellitus
ECG	-	Electrocardiogram
ECHO	-	Echocardiogram
LAD	-	Left Anterior Descending Artery
LCX	-	Left Circumflex coronary artery
LMCA	-	Left Main Coronary artery
LV	-	Left Ventricle
MI	-	Myocardial Infarction
MR	-	Mitral Regurgitation
RCA	-	Right Coronary Artery
RV	-	Right Ventricle
RWMA	-	Regional Wall Motion Abnormalities
SHT	-	Systemic Hypertension
TMT	-	Tread Mill Test
CAD	-	Coronary Artery Disease
VSR	-	Ventricular Septal Rupture
2-D	-	2 Dimensional

CABG	-	Coronary Artery Bypass Graft
LBBB	-	Left Bundle Branch Block
RBBB	-	Right Bundle Branch Block
BNP	-	B type Natriuretic peptide
VF	-	Ventricular Fibrillation
VT	-	Ventricular tachycardia
RAO	-	Right Anterior Oblique
LAO	-	Left Anterior Oblique
A4C	-	Apical 4 chamber
A2C	-	Apical 2 chamber
PSLAX	-	Parasternal Long axis
PSSAX	-	Parasternal Short axis
CCS	-	Canadian cardiovascular society
NYHA	-	Newyork Heart Association
STEMI	-	ST elevation myocardialinfarction
NSTEMI	-	Non ST elevation myocardial infarction

BIBLIOGRAPHY

1. Rod JL, Bakst A, Gotsman MS, Lewis BS: Isolated circumflex coronary artery obstruction. Isr J Med Sci 16: 588, 1980

2. Moskowitz RM, Kronzon I, Schloss M, Glassman E: The clinical and angiographic spectrum of isolated, nondominant left circumflex coronary artery. catherCardiovasc diagn2. 281 (1976)

3. Stadius ML, Maynard C, Fritz JK, Davis K, Ritchie JL, Shechan F, Kennedy JW: Coronary anatomy and left ventricular function in the first 12 **hours** of acute myocardial infarction:The Westem Washington randomized intracoronary streptokinase trial. Circulation 72.292 (I 985)

4. Bairey CN, Shah PK, Lew AS, Hulse**S:** Electrocardiographic differentiation of occlusion of the left circumflex versus right coronary artery as a cause of inferior acute myocardial infarction. ***Am .I*** Cardiol60,456 (1987)

5. Morrow DA, Antman EM, Parsons L *et al.* Application of the TIMI risk score for ST-elevation MI in the National Registry of Myocardial Infarction 3. *JAMA* 2001; **286**: 1356–1359

6. Killip T, and Kimball JT: Treatment of myocardial infarction in a coronary care unit: a two year experience of 250 patients. American Journal of Cardiology 1967; 20: 457-464

7. Singh M, Reeder GS, Jacobsen SJ Weston S, Killian J, Roger VL. Scores for post-myocardial infarction risk stratification in the community. *Circulation* 2002; **106**: 2309–2314

8. *Granger CB, Goldberg RJ, Dabbous OH et al. for the Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the global registry of acute coronary events. Arch Intern Med 2003;163:2345–2353*

9. Dunn RF, Newman HN, Bemstein L, Hams PJ, Roubin GS, Morris J, Kelly DT The clinical features of isolated left circumflex coronary artery disease. Circulation 69,477 (1984)

10. Perloff JK: The recognition of strictly posterior myocardial infarction by conventional scalar electrocardiography. Circulation 30: 706, 1964

11. Tulloch JA: The electrocardiographic features of high posterolateral myocardial infarction. Br Heart J 14: 379, 1952

12. Lee KL, Woodlief LH, Topol EJ *et al*. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41 021 patients. GUSTO-I Investigators.*Circulation* 1995; **91**:1659–1668.

13. Schuchert A, Hamm C, Scholz J, Klimmeck S, Goldmann B, Meinertz T. Prehospital testing for troponin T in patients with

suspected acute myocardial infarction. *Am Heart J* 1999; **138**: 45–48.

14. Burch GE, Giles TD, Colcolough HL. Ischemic cardiomyopathy.*Am Heart J* 1970; **79**: 291–292.

15. Richardson P, McKenna W, Bristow M *et al*. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. *Circulation* 1996; **93**: 841–842.

16. Pagano D, Lewis ME, Townend JN, Camici PG, Bonser RS. Coronary revascularisation for post-ischaemic heart failure: how myocardial viability affects survival. *Heart* 2000; **83**: 456–461.

17. Hathaway WR, Peterson ED, Wagner GS *et al*. Prognostic significance of the initial electrocardiogram in patients with acute myocardial infarction. GUSTO-I Investigators. Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries.*JAMA* 1998; **279**: 38–91.

18. Fiol M, Cygankiewicz I, Guindo J *et al*. Evolving myocardial infarction with ST elevation: ups and downs of ST in different leads identifies the culprit artery and location of the occlusion. *Ann NoninvasiveElectrocardiol* 2004; **9**: 180–186.

19. Sadanandan S, Hochman S, Kolodziej A *et al*. Clinical and angiographic characteristics of patients with combined anterior and inferior ST segment elevation in the initial ECG during acute myocardial infarction.*Am Heart J* 2003; **146**: 653–661.

20. Wellens HJ, Gorgels A, Doevendans PA. *The ECG in Acute Myocardial Infarction and Unstable Angina*, 2003. Boston: Kluwer Academic Publishers

21. Fiol M, Carillo A, Cygankiewicz I *et al*. New criteria based on ST changes in 12 leads surface ECG to detect proximal vs. distal right coronary artery occlusion in case of an acute inferoposterior myocardial infarction. *Ann NoninvasiveElectrocardiol*2004; **9**: 383–389.

22. British Heart Foundation. *Coronary Heart Disease Statistics*, 2004. London: British Heart Foundation.

23. Elsaesser A, Hamm CW. Acute coronary syndrome: the risk of being female. *Circulation* 2004; **109**: 565–567.

24. Weiss R, Dziura J, Burgert TS *et al*. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004; **350**: 2362–2374.

25. Falk E, Shah PK, Fuster V. Atherothrombosis and thrombosis-prone plaques. In: Fuster V, Alexander RW, O'Rourke RA, *et al*., eds. *Hurst's the Heart*, 2004. New York: McGraw-Hill, pp. 1123–1139.

26. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003; **348**: 383–393.

27. WHO. *World Health Report 2002; Reducing Risk, Promoting Healthy Life*, 2002. Geneva: World Health Organization.

28. Ninomiya JK, L'Italien G, Criqui MH, Whyte JL, Gamst A, Chen RS. Association of the metabolic syndrome with history of myocardial infarction and stroke in the third national health and nutrition examination survey. *Circulation* 2004; **109**: 42–46.

29. Vaughan CJ, Gotto AM, Jr. Update on statins: 2003. *Circulation* 2004; **110**: 886–892.

30. Barker DJ. Fetal origins of coronary heart disease.*Br Med J* 1995; **311**: 171–174.

31. Yusuf S, Hawken S, Ounpuu S *et al*. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case–control study. *Lancet* 2004; **364**: 937–952.

32. Braunwald E. Unstable angina.A classification.*Circulation* 1989; **80**: 410–414.

33. Cannon CP, McCabe CH, Stone PH *et al*. The electrocardiogram predicts one-year outcome of patients with unstable angina and non-Q wave myocardial infarction: results of the TIMI III Registry ECG Ancillary Study.Thrombolysis in Myocardial Ischemia.*J Am Coll Cardiol* 1997; **30**: 133–140.

34. Bean WB. Masquerades of myocardial infarction.*Lancet* 1977; **1**: 1044–1046

35. GilliamLD,Hogan, Foyale RA et al A comparison of quantitative echocardiographic methods for delineating inarct induced abnormal wall motion. Circulation 1984:63; 739-746.

36. Hamby RI, Gupta MP, YoungMW: Clinical and hemodynamic aspects of single vessel coronary artery disease. Am Heart J 85: 458, 1973

37. Gorlin R: Coronary anatomy. MaJor.ProblIntern Med 11: 40, 1976

38. Dunn WJ, Edwards JE, Pruitt RD: The electrocardiogram in infarction of the lateral wall of the left ventricle: a clinicopathological study. Circulation 14: 540, 1956

39. James TN: The coronary circulation and conduction system in acute myocardial infarction. Prog Cardiovasc Dis 10: 410, 1968

40. Miller RR, DeMaria AN, Vismara LA, Salel AF, Maxwell KS, Amsterdam E, Mason DT: Chronic stable inferior infarction: unsuspected harbinger of high-risk proximal left coronary arterial obstruction amenable to surgical revascularization. Am J Cardiol 39: 954, 1977

41. Schlesinger MT: Relation of anatomic pattern to pathologic conditions of the coronary arteries. Arch Pathol 30: 403, 1940

42. Bakst A, Lewis BS, Mitha AS, Gotsman MS. Isolated obstruction of the right coronary artery. Chest 65: 18, 1974

43. Gensini GG: Coronary arteriography. In Braunwald E, editor:Heart disease.A textbook of cardiovascular medicine. Philadelphia, 1980, W.B. Saunders Company, p 211

44. Braat SH, Gorgels APM, Bar **FW,** Wellens HJT Value of the ST-T segment in lead V4R in inferior wall acute myocardial infarction to predict the site of coronary arterial occlusion. ***Am***.Cardiol62, 140 (1988)

45. Brembilla-Perrot B, Temer De La Chaise **A,** Isaaz K, Pemot**C:** The tall R wave in lead **V** I in posterior myocardial infarction: A reciprocal sign or a His-Purkinje conduction disturbance? Pace 12, 1670 (1989)